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Toxicity of 45 Organic Herbicides to Cattle, Sheep, and Chickens

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Toxicity of 45 Organic Herbicides to Cattle, Sheep, and Chickens

By J. S. PALMER, *veterinary medical officer, Veterinary Sciences Research Division, Agricultural Research Service*^{1 2}

SUMMARY

Results of studies of the toxicity of 45 formulated organic herbicides to cattle, sheep, and chickens are presented. These herbicides are used extensively in this country. All such compounds have had registered recommended uses for various agricultural uses with three having this registration currently discontinued. A total of 238 yearling cattle, 333 one- to two-year-old sheep, and 1,430 six-week-old chickens were studied.

An arbitrary yield of forage and rate of consumption were selected to evaluate the hazard to cattle, sheep, and chickens likely to exist under the most severe conditions of use.

Repeated doses of the herbicides were administered in gelatin capsules or as water-diluted solutions by drench or pipette. The usual period of study was 10 days, or until toxicologic effects appeared.

The signs of poisoning by most of the herbicides included anorexia and weight loss or reduced weight gains. In many instances digestion was impaired by congestion or redness of the intestinal mucosa. Macroscopic lesions on necropsy varied widely between herbicides and occasionally among test animals dosed by varying quantities of the same herbicide. Prominent and distended cranial vessels were often associated with depression and ataxia before death. The liver and kidneys were most frequently involved.

The most common or moderate rates of application of many of these herbicide formulations are not a hazard to cattle, sheep, or chickens. The maximum rates of some approach or surpass a hazardous concentration in one or more of the test species. The minimum or single recommended rate for a few of these herbicides would present a similar hazard.

INTRODUCTION

The Veterinary Sciences Research Division, Agricultural Research Service, investigates the toxicologic effects of agricultural chemicals to farm animals. It has previously reported on the toxicity of 29 herbicides to cattle, sheep, and

chickens.³ The procedure used in these studies was generally short term—10 or fewer consecutive daily doses. This regimen was considered a type of exposure that might be expected when these animals consumed relatively large quantities of the organic herbicides for a short time. The likelihood of poisoning was assessed in relation to the toxic dosage to each animal

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² Acknowledgment is made to personnel of the Plant Science Research Division of ARS and Pesticides Regulation Division, Environmental Protection Agency (formerly of ARS) for their suggestions, revisions, and comments.

³ PALMER, J. S., and RADELEFF, R. D. THE TOXICITY OF SOME ORGANIC HERBICIDES TO CATTLE, SHEEP, AND CHICKENS. U.S. Dept. Agr. Prod. Res. Rpt. 106, 26 pp. 1969.

species and the amounts of the herbicide recommended for application to vegetation.

These same testing procedures were continued for this present report. Thus the same criteria can be used for evaluating each organic herbicide. Forty-five additional herbicides were chosen for the current studies, based on the extent of usage of the herbicides, both past and present, in agriculture. All have been registered for agricultural use and most retain current registration with the Pesticides Regulation Division, Environmental Protection Agency. Therefore, toxicity data from all test animals exposed to each herbicide have been included. This inclusion allows a more complete study of the effects of various chemicals to the test animals. Two or more salt or ester formulations of the commonly used chlorophenoxy herbicides were tried. Other herbicides, grouped as to similarity of chemical structure, were chlorinated aliphatic acid, amide, phenyl urea, carbamate, thiocarbamate, arsenical, substituted dinitroaniline, dipyridyl, phthalamic acid, and miscellaneous compounds.

The impetus for toxicologic studies to animals relates ultimately to the direct and indirect influence on man. In a recent review, only eight organic herbicides were proved to have caused human poisoning.⁴ For every fatal case, however, there are an estimated 100 nonfatal cases because there is no general rule of reporting their occurrence. The degree of hazard to man and animals from exposure to an organic herbicide depends upon many complex factors, in-

cluding its extent of misuse. Although the thorough examination of any single factor is not completely reliable, acute oral toxicity studies, involving relatively large doses over a short period of time, lend themselves to an assessment of potential injury from other types of exposure.

In studies at the Toxicological Research Laboratory, Kerrville, Tex., an observable sign of abnormal function or behavior of the test animal was considered as an adverse effect or poisoning. This effect was manifested by anorexia (lack or loss of appetite for feed—either partial or complete) in its mildest form to convulsions, sudden death, or both. Other animals during the trial period had no apparent ill effects, including anorexia. However, a decrease in total body weight was attributed to interference with feed utilization. A 5-percent or more weight loss in cattle or sheep or a 5-percent or more reduced weight gain in chickens was considered significant.

With the appearance of a mandibular area enlargement in cattle and sheep, following doses by drench, the continuation of the regimen was usually carried out by doses incorporated in gelatin capsules. All such cases were documented under each organic herbicide studied. All of these were classified as "irritation effect only" because others of the same species failed to exhibit adverse effects at the same or the next higher dosage levels. Other animals, more severely affected, were considered poisoned because of other signs and conditions produced.

INTERPRETATION OF HAZARD

To relate the toxic dosages found for cattle, sheep, and chickens to the application rates recommended for each herbicide,⁵ the probable amounts that could be consumed daily from

recently sprayed fields or pastures were calculated. In these calculations, neither the influence of environmental factors nor the decomposition rates of the herbicides were considered.

An arbitrary, although realistic, yield of 0.1 pound of air-dry forage per square foot of area was selected, which is the equivalent to approximately 2 tons per acre. This quantity would represent a high-quality, improved pasture (with adjustment for local conditions). A sparse cover of vegetation would allow more of the herbicide to reach the ground and be unavailable to animals, whereas a more lush cover

⁴ HAYES, W. J., JR. PESTICIDES AND HUMAN TOXICITY. In *Biological Effects of Pesticides in Mammalian Systems*. N.Y. Acad. Sci. Ann. 160(1): 40-54. 1969.

⁵ U.S. DEPARTMENT OF AGRICULTURE. U.S.D.A. SUMMARY OF REGISTERED AGRICULTURAL PESTICIDE CHEMICAL USES. HERBICIDES, DEFOLIANTS, DESSICANTS, PLANT REGULATORS. Ed. 3, v. 1, 227 pp. [Includes replacement pages to Jan. 16, 1970.] 1968.

would tend to hold more of the material available. In the latter case, however, less of the forage of the area would be consumed in any one day.

Further assumptions were: (1) That an animal would consume, as forage, 3 percent of its body weight each day; and (2) that all the chemical formulation applied would adhere to the vegetation. Although this latter is never actually the case, this assumption gives the maximum exposure to be expected.

An application of 1 pound of chemical to 1 acre of land provides 10.4 milligrams for each square foot. We may simplify the whole calculation to a single statement that *1 pound actual of herbicide per acre provides a 7-milligram per kilogram (mg./kg.) dosage* to the animal under the conditions here assumed to exist. Each 2.2 pounds of animal weight equals 1 kilogram or 1,000 grams. In turn, 1 pound equals 454 grams. The equivalent of 1,000 mg./kg. is 454 milligrams per pound (mg./lb.).

EXPERIMENTAL ANIMALS

The cattle and sheep treated were obtained directly from local farmers and ranchers or through local auctions and were commercial stock. Cattle were of mixed breeding and sex, approximately 9 to 16 months old, and were classified as yearlings. Sheep were ewes and wethers of predominantly Delaine breeding. The cattle and sheep were maintained in open pens and provided with rations of grain concentrates and hay. Mineral supplement and water were allowed as free choice.

Most chickens were White Leghorns of mixed sex, hatched from pathogen-free eggs to overcome inherent endemic disease lesions masking those produced by the organic herbicides. All chickens were held in brooder or grower pens for 6 weeks, first on a commercial starting feed and later on a growing mash; then the trials were started. Before each experiment was started, each of the chickens was weighed and legbanded, then placed with four others in isolated cages. All five were treated at the same dosage level of the organic herbicide. An additional chicken in each cage, also weighed and legbanded, served as a control.

Cattle and sheep were routinely studied without parallel controls. Animals treated at less than toxic dosages were considered to gain weights at rates comparable with rates for untreated animals with no other alteration of behavior. To investigate these observations further, 10 yearlings and 14 sheep, equally divided as to sex and age, were purchased from a common environmental background (tables 1 and 2). A prolonged period of acclimatization to feed and restricted pens was allowed. Ten-day exposure periods with four organic herbicides in cattle and five in sheep were carried out in which total feed consumption and its effect on weight was measured. Dosage levels were selected as those causing a loss of weight previously in one or more animals. Results of this special trial varied between paired animals or between species exposed to each herbicide. Anorexia, metabolic interference, or increased utilization were the apparent effects of the herbicides. The variance in individual tolerance in this trial appeared to be the greatest single factor to the adverse effects at the minimum toxic dosages.

EXPERIMENTAL MATERIALS AND DOSAGES

The various organic herbicides studied were all in commercially available formulations. Dosages were calculated on a mg./kg. basis for the active ingredient(s) of each chemical formulation to the body weight of the test animals. Dosages were periodically recalculated in chronic studies as the weight of the animals changed.

Cattle and sheep were dosed by drench or capsule. Drenching was resorted to because of a shortage of gelatin capsules and fairly large daily doses. It consisted of diluting the calculated formulation with water, administering it by use of a syringe, and following this with a water rinse. This method of dosing was restricted to test animals because of the irritation effects of

the chemical formulations on the mucosa of the upper digestive tract. This was especially evident in cattle, but occasionally in sheep. A balling gun, with the formulations in appropriate-size gelatin capsules, was used where circumstances permitted.

Chickens were dosed by water-diluted formu-

lation by use of pipettes or by formulations in gelatin capsules. The treated chickens and the control in each cage were handled similarly; the controls were given untreated water or empty capsules.

The method used to select the number of doses administered and the dosage rates for each test

TABLE 1.—*Effects of various organic herbicides administered as minimum toxic dosages to cattle for 10 days as related to feed consumption and utilization*

Feed consumption			Body weight				Remarks
Herbicide	Daily range	Total	Initial	Final	Differential		
	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Percent</i>	
A.....	0.3 - 4.5	20.5	275	262	-13	-5	Partial anorexia.
A.....	.3 - 5.3	26.2	370	365	- 5	-1	Do.
B.....	3.9 - 5.5	52.1	330	320	-10	-3	Metabolic interference.
B.....	2.5 - 4.0	46.2	295	310	15	5	Increased utilization.
C.....	4.8 - 5.3	51.3	355	355	0	0	Metabolic interference.
C.....	1.1 - 2.6	18.2	340	340	0	0	Partial anorexia.
D.....	0 - 4.5	8.1	340	330	-10	-3	Anorexia.
D.....	0 - 3.3	12.6	292	284	- 8	-3	Do.
Control.....	3.5 - 4.5	41.5	362	362	0	0	No remark.
Control.....	.4 - 5.3	33.0	365	370	5	1	Do.

TABLE 2.—*Effects of various organic herbicides administered as minimum toxic dosages to sheep for 10 days as related to feed consumption and utilization*

Feed consumption			Body weight				Remarks
Herbicide	Daily range	Total	Initial	Final	Differential		
	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Pounds</i>	<i>Percent</i>	
A-----	1.1 - 1.3	12.0	70.5	75.0	4.5	6	Improved utilization.
A-----	1.1 - 1.4	13.3	68.5	74.0	5.5	8	Do.
B-----	1.1 - 1.4	13.3	60.0	65.0	5.0	8	Do.
B-----	1.4	14.4	66.0	63.0	-3.0	-5	Metabolic interference.
C-----	.8 - 1.1	9.7	61.5	65.5	4.0	7	Improved utilization.
C-----	.1 - 1.3	5.5	61.0	58.5	-2.5	-4	Partial anorexia.
D-----	.1 - 1.0	3.5	69.0	67.0	-2.0	-3	Do.
D-----	0 - 1.3	8.1	67.5	69.5	2.0	3	None.
E-----	0 - 1.0	1.7	63.0	55.5	-7.5	-12	Anorexia.
E-----	1.3 - 1.4	13.1	73.0	74.5	1.5	2	Metabolic interference.
Control-----	.7 - 1.0	9.1	60.0	62.5	2.5	4	None.
Control-----	.5 - 1.0	7.3	65.0	66.0	1.0	2	Do.
Control-----	.3 - 0.8	5.4	59.0	59.0	0	0	No effect.
Control-----	.4 - 1.0	7.4	66.0	64.0	-2.0	-3	Do.

animal involved several variables. The initial dosage rate was usually based on trial and error. When a toxic dosage was found, additional dosages above and below this rate were applied to other cattle, sheep, and chickens. Where a step-by-step increase of dosages indicated increased toxicity, repetition of individual dosages was not considered essential.

After each trial was completed, usually 10 days or less, each surviving animal was weighed;

the weight change was expressed as the percentage of initial, or preexposure, weight. Subsequently, each was observed for a minimum period of 60 days for signs of chronic effects. Animals that died or were sacrificed during the course of the dosing or afterwards were necropsied. Those sacrificed were moribund and death was considered imminent. Specimens for histopathological examination were collected for later study.

RESULTS

Chlorophenoxy Compounds

(2,4-dichlorophenoxy) acetic acid (2,4-D), dimethylamine salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 3). Cattle had weight loss and chickens had reduced weight gains at 100 mg./kg. Although sheep were not affected at 100 mg./kg., one was poisoned and died after four doses at 175, and two died after seven doses at 250. Contrastingly, cattle had only weight losses and chickens only reduced weight gains at these increased dosages. Three of five chickens in a group died at 500 mg./kg., and survivors in the group had reduced weight gains.

Sheep showed anorexia and progressive weakness before death; chickens were depressed before death. Other chickens and cattle affected had no notable untoward reactions.

At necropsy, lesions were limited to a friable liver and reddened intestinal mucosa in two of three sheep. There were also a swollen spleen, a reddened respiratory mucosa, and congested kidneys in one that died at 250 mg./kg. Chickens had enlarged, congested kidneys.

Application rates for 2,4-D salts range from 0.42 to 6 pounds actual per acre. These rates would not be hazardous for the three test species.

(2,4-dichlorophenoxy) acetic acid (2,4-D), 2-ethylhexyl ester

All test animals were dosed by capsule (table 4). Three of four yearlings were poisoned after six to 14 doses at 250 mg./kg. One sheep had weight losses at 50 mg./kg. and two sheep at 100. Chickens had reduced weight gains at 250

TABLE 3.—*Results of multiple oral dosing of cattle, sheep, and chickens with (2,4-dichlorophenoxy)acetic acid (2-4-D), dimethylamine salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	--do-----	Do.
100-----	10	--do-----	Do.
100-----	10	--do-----	7-percent weight loss.
175-----	10	--do-----	Do.
250-----	10	--do-----	8-percent weight loss.
Sheep:			
100-----	10	--do-----	NIE.
100-----	10	--do-----	Do.
175-----	4	--do-----	Poisoned after 2 and died.
250-----	7	--do-----	Poisoned after 4 and died.
250-----	7	--do-----	Poisoned after 3 and died.
Chickens: ³			
25-----	10	Pipette---	59-percent weight gain.
50-----	10	--do-----	Do.
100-----	10	--do-----	38-percent weight gain.
175-----	10	--do-----	30-percent weight gain.
250-----	10	--do-----	Do.
375-----	10	--do-----	Do.
500-----	10	--do-----	3 died after 2 to 7 doses, 26-percent weight gain in survivors.
Controls--	-----	-----	57-percent weight gain.

¹ DMA-4®, 49.6 percent water soluble concentrate, Dow Chemical Co., Midland, Mich.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

TABLE 4.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with (2,4-dichlorophenoxy)acetic acid (2,4-D), 2-ethylhexyl ester*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
100-----	10	NIE.
100-----	10	Do.
250-----	9	Do.
250-----	10	5-percent weight loss.
250-----	14	Poisoned and died.
250-----	6	Do.
Sheep:		
25-----	10	NIE.
25-----	10	Do.
50-----	10	7-percent weight loss.
100-----	10	NIE.
100-----	10	7-percent weight loss.
100-----	10	8-percent weight loss.
250-----	50	NIE.
250-----	56	Do.
250-----	10	7-percent weight loss.
250-----	16	Poisoned after 14 and died.
250-----	8	Poisoned and died.
250-----	6	Poisoned after 5 and died.
500-----	10	Poisoned and died.
500-----	5	Do.
Chickens: ³		
100-----	10	57-percent weight gain.
250-----	10	42-percent weight gain.
500-----	10	36-percent weight gain.
Controls-----		59-percent weight gain.

¹ Weed Rhap®, 69.47 percent emulsifiable concentrate, Hercules, Inc., Wilmington, Del.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

and 500 mg./kg. The biochemical effects of this herbicide in cattle and sheep were studied in conjunction with these trials. The alterations of the magnesium:calcium ratios and blood urea nitrogen levels after repeated daily doses have been described.⁶

⁶ HUNT, L. M., GILBERT, B. N., and PALMER, J. S. EFFECTS OF A HERBICIDE, 2-ETHYL HEXYL ESTER OF 2,4-D ON MAGNESIUM:CALCIUM RATIOS AND BLOOD UREA NITROGEN LEVELS IN SHEEP AND CATTLE. *Bul. Environmental Contamination and Toxicol.* 5(1): 54-60. 1970.

Signs of poisoning in cattle and sheep were anorexia, depression, and ataxia (failure of muscular coordination).

At necropsy, the thyroid, kidneys, and liver were generally congested and enlarged. The intestinal mucosa was reddened and there were a number of cases of rumen stasis characterized by bright, undigested feed. In animals having ataxia before death, blood vessels of the brain were found engorged. The lungs were often engorged with blood and the respiratory tract was congested and filled with froth. The spleen was noted to be thickened on occasion.

The application rates for 2,4-D esters range from 0.42 to 6 pounds actual per acre. These rates would not be hazardous for the three test species.

(2,4,5-trichlorophenoxy) acetic acid (2,4,5-T), 2-ethylhexyl ester

All test animals were dosed by capsule (table 5). A yearling was adversely affected by weight loss at 100 mg./kg., and a sheep was poisoned and died 4 days after 10 doses at 50. Chickens had reduced weight gains at 100 mg./kg.

The only sign of poisoning in cattle and sheep was anorexia, which became apparent initially on the day before or, in some cases, on the day of death.

At necropsy, lesions were generally limited to the respiratory and gastrointestinal tracts, in which the lungs were congested and the mucosa was reddened. The liver was often swollen and the kidneys were engorged with blood. In the yearling that died at 250 mg./kg. and the sheep at 500, hemorrhages were seen in the subcutaneous tissues. The three chickens had swollen kidneys, congested liver, and reddened intestinal mucosa.

Application rates for 2,4,5-T esters range from 0.5 to 4.5 pounds actual per acre. These rates would not be hazardous for the three test species.

(2,4,5-trichlorophenoxy) acetic acid (2,4,5-T), triethylamine salt

Cattle were dosed by capsule, sheep by capsule or drench, chickens by pipette (table 6). A yearling had weight loss at 100 mg./kg., and a

TABLE 5.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), 2-ethylhexyl ester¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
50-----	10	NIE.
50-----	40	Do.
100-----	10	Do.
100-----	10	8-percent weight loss.
250-----	7	Poisoned and died.
Sheep:		
25-----	10	NIE.
50-----	10	Do.
50-----	10	Do.
50-----	10	7-percent weight loss.
50-----	10	12-percent weight loss, died 4 days after last dose.
100-----	10	NIE.
100-----	10	Poisoned after 2 and died 12 days after last dose.
175-----	7	Poisoned and sacrificed.
250-----	6	Poisoned after 4 and died.
500-----	5	Poisoned after 3 and died.
Chickens: ³		
10-----	10	52-percent weight gain.
25-----	10	51-percent weight gain.
50-----	10	55-percent weight gain.
100-----	10	45-percent weight gain.
250-----	10	39-percent weight gain.
375-----	10	1 died after 9, 16-percent weight gain in survivors.
500-----	10	2 died after 8 and 10, 23-percent weight gain in survivors.
Controls-----		54-percent weight gain.

¹ Brush Rhap®, 63.5 percent emulsifiable concentrate, Hercules, Inc., Wilmington, Del.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

sheep was poisoned after five doses at 50. One chicken died at 50 mg./kg., but that dosage had no adverse affects on the survivors in that group.

Signs of poisoning in cattle and sheep were anorexia, depression, and weakness.

At necropsy, congestion of the lungs and reddened respiratory mucosa were dominant; the liver and kidneys were enlarged and blood engorged. The thyroid was swollen and con-

TABLE 6.—Results of multiple oral dosing of cattle, sheep, and chickens with (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), triethylamine salt¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	17-percent weight loss.
175-----	4	..do-----	Poisoned after 1 and survived.
250-----	4	..do-----	Poisoned after 3 and died 2 days after last dose.
Sheep:			
25-----	10	Capsule--	NIE.
25-----	10	..do-----	Do.
50-----	10	..do-----	Do.
50-----	10	..do-----	Poisoned after 5 and survived, 6-percent weight loss.
100-----	10	..do-----	NIE.
100-----	10	..do-----	6-percent weight loss.
100-----	7	Drench--	Poisoned after 2 and died 2 days after last dose.
175-----	4	Capsule--	Poisoned and died.
250-----	5	..do-----	Do.
250-----	4	..do-----	Do.
Chickens: ³			
25-----	10	Pipette--	55-percent weight gain.
50-----	10	..do-----	1 died after 10, 55-percent weight gain in survivors.
100-----	10	..do-----	35-percent weight gain.
100-----	10	..do-----	1 died after 10, 39-percent weight gain in survivors.
250-----	10	..do-----	19-percent weight gain.
250-----	10	..do-----	2 died after 9, 35-percent weight gain in survivors.
375-----	10	..do-----	30-percent weight gain.
375-----	10	..do-----	3 died after 2 to 5, 16-percent weight gain in survivors.
500-----	6	..do-----	All died after 2 to 6.
Controls-----			45-percent weight gain.

¹ Veon 245®, 56.1 percent water soluble concentrate, Dow Chemical Co., Midland, Mich.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

gested and there were petechiae and hemorrhages in the subcutaneous tissue and muscles. The congested intestinal mucosa was associated with rumen stasis. Lesions in chickens involved the liver, kidneys, and intestinal mucosa; all appeared congested and swollen.

Application rates for 2,4,5-T amine salts range from 0.5 to 4.5 pounds actual per acre. These rates would not be hazardous for the three test species, but a 50-percent increase would be hazardous for sheep.

4-[(4-chloro-o-tolyl)oxy]butyric acid (MCPB), sodium salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 7). One sheep was poisoned after five doses at 50 mg./kg. One yearling was poisoned after one dose and another after two doses at 100 mg./kg. One chicken died at 100 mg./kg., and survivors in that group had reduced weight gains.

Signs of poisoning in cattle and sheep were anorexia, depression, uncoordinated gait, and weakness.

At necropsy, there were acute reddened respiratory mucosa, friable and engorged liver, congested kidneys, redness of intestinal mucosa, and hyperemic mesentery lymph nodes. The cerebral vessels were engorged and there were petechiae in the subcutaneous tissue. Swollen kidneys and spleen and reddened intestinal mucosa were seen in the two poisoned chickens.

The only application rate for MCPB is for peas at 1.5 pounds actual per acre. This rate would not be hazardous for the three test species.

[(4-chloro-o-tolyl)oxy]acetic acid (MCPA), sodium salt

Cattle were dosed by capsule, sheep by drench, chickens by pipette (table 8). One sheep was poisoned after five doses at 100 mg./kg. and a yearling after three doses at 175. Two chickens died after one and 10 doses at 500 mg./kg., and survivors in that group had reduced weight gains.

One yearling showed diarrhea and anorexia as signs of poisoning, whereas other cattle and sheep showed only anorexia.

TABLE 7.—Results of multiple oral dosing of cattle, sheep, and chickens with 4-[(4-chloro-o-tolyl)oxy]butyric acid, sodium salt¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	--do-----	Do.
100-----	2	--do-----	Poisoned and died.
100-----	1	--do-----	Poisoned and survived, 28-percent weight loss.
Sheep:			
25-----	10	--do-----	NIE.
25-----	10	--do-----	Do.
50-----	10	--do-----	7-percent weight loss.
50-----	10	--do-----	Poisoned after 5 and survived, 8-percent weight loss.
100-----	8	--do-----	Poisoned after 5 and died.
Chickens: ³			
50-----	10	Pipette--	47-percent weight gain.
100-----	10	--do-----	1 died after 10, 35-percent weight gain in survivors.
250-----	10	--do-----	1 died after 6, 37-percent weight gain in survivors.
Controls--	-----	-----	50-percent weight gain.

¹ Can-Trol®, 23.5 percent water soluble concentrate of MCPB, Rhodia, Inc., Chipman Division, New Brunswick, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

At necropsy, the one sheep had reddened small intestinal mucosa and swollen edematous adjacent lymph nodes, and its spleen was thickened. Chickens had congested liver and kidneys, enlarged spleen, and reddened intestinal mucosa.

Application rates for MCPA range from 0.13 to 3 pounds actual per acre. These rates would not be hazardous for the three test species.

[(4-chloro-o-tolyl)oxy]acetic acid (MCPA), dimethylamine salt

Cattle were dosed by capsule, sheep by capsule or drench, chickens by pipette (table 9).

TABLE 8.—Results of multiple oral dosing of cattle, sheep, and chickens with [(4-chloro-o-tolyl)oxy]acetic acid, sodium salt ¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
100-----	10	Capsule--	NIE.
100-----	10	..do-----	Do.
175-----	10	..do-----	Poisoned after 3 and survived, 11-percent weight loss.
250-----	10	..do-----	Poisoned after 8 and survived, 18-percent weight loss.
Sheep:			
50-----	10	Drench--	NIE.
50-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Poisoned after 5 and survived, 11-percent weight loss.
175-----	10	..do-----	NIE.
175-----	10	..do-----	6-percent weight loss.
250-----	4	..do-----	Poisoned after 3 and died.
Chickens: ³			
100-----	10	Pipette--	51-percent weight gain.
250-----	10	..do-----	47-percent weight gain.
500-----	10	..do-----	2 died after 1 and 10, 30-percent weight gain in survivors.
Controls-----			50-percent weight gain.

¹ MCPA Sodium Salt®, 24.2 percent water soluble concentrate, Rhodia, Inc., Chipman Div., New Brunswick, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

Although one sheep had a weight loss at 100 mg./kg., two others were unaffected at 175 and 250. However, other sheep were poisoned and died at 250 and 375 mg./kg. Two yearlings had a similar weight loss at 175 mg./kg. One group of chickens had reduced weight gains at 10 mg./kg., but that dosage had no adverse effects on another group. One chicken died at 100 mg./kg.

Mildly affected cattle and sheep had a metabolic interference with feed utilization as ap-

TABLE 9.—Results of multiple oral dosing of cattle, sheep, and chickens with [(4-chloro-o-tolyl)oxy]acetic acid, dimethylamine salt ¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
100-----	10	Capsule--	NIE.
100-----	10	..do-----	Do.
175-----	10	..do-----	5-percent weight loss.
175-----	10	..do-----	Do.
250-----	10	..do-----	Poisoned after 8 and survived, 16-percent weight loss.
Sheep:			
50-----	10	..do-----	NIE.
50-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	Drench--	7-percent weight loss.
175-----	10	Capsule--	NIE.
250-----	10	..do-----	Do.
250-----	7	Drench--	Poisoned after 5 and died. ³
375-----	3	Capsule--	Poisoned and died.
Chickens: ⁴			
10-----	10	Pipette--	56-percent weight gain.
10-----	10	..do-----	33-percent weight gain.
25-----	10	..do-----	28-percent weight gain.
25-----	10	..do-----	26-percent weight gain.
50-----	10	..do-----	27-percent weight gain.
50-----	10	..do-----	26-percent weight gain.
100-----	10	..do-----	1 died after 5, 38-percent weight gain in survivors.
250-----	10	..do-----	1 died after 7, 35-percent weight gain in survivors.
500-----	10	..do-----	3 died after 4 to 8, 36-percent weight gain in survivors.
Controls-----			43-percent weight gain.

¹ Chipman MCPA Amine®, 52.2 percent water soluble concentrate, Rhodia, Inc., Chipman Div., New Brunswick, N.J.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

petite appeared to be normal during the trial periods, but with loss of weight. Other more severely affected test animals showed anorexia.

A sheep was poisoned and died, but before this, it had a mandibular swelling caused from chemical irritation due to drenching. This was considered to have little, if any, effect on MCPA toxicity to sheep. In a sheep that was acutely poisoned and died, convulsions preceded death.

At necropsy, the abomasal and intestinal mucosa was reddened, the liver was congested and friable, and the cranial vessels were engorged.

Application rates for MCPA range from 0.13 to 3 pounds actual per acre. These rates would not be hazardous for the three test species.

4-(2,4-dichlorophenoxy)butyric acid (2,4-DB), dimethylamine salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 10). One sheep was poisoned after five doses at 50 mg./kg. but survived 10 doses, with weight loss. Another sheep was not affected by the same dosage. Two yearlings were poisoned after two doses at 100 mg./kg. and one died. Chickens had reduced weight gains at 250 mg./kg.

Signs of poisoning in cattle and sheep were anorexia, weakness, and depression. In the one yearling that was acutely poisoned and died, diarrhea followed by muscular spasms preceded death.

At necropsy, lesions were limited to the digestive system, with congestion of the intestinal mucosa and engorged mesenteric vessels.

Application rates for 2,4-DB range from 0.22 to 2 pounds actual per acre. These rates would not be hazardous for the three test species.

TABLE 10.—*Results of multiple oral dosing of cattle, sheep, and chickens with 4-(2,4-dichlorophenoxy)butyric acid, dimethylamine salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
25-----	10	Capsule--	NIE.
50-----	10	..do....	Do.
50-----	10	..do....	Do.
100-----	10	..do....	Poisoned after 2 and survived, 7-percent weight loss.
100-----	2	..do....	Poisoned and died.
Sheep:			
25-----	10	..do....	NIE.
25-----	10	..do....	Do.
50-----	10	..do....	Do.
50-----	10	..do....	Poisoned after 5 and survived, 7-percent weight loss.
100-----	10	..do....	Poisoned after 5 and died 3 days after last dose, 25-percent weight loss.
Chickens: ³			
100-----	10	Pipette--	46-percent weight gain.
250-----	10	..do....	45-percent weight gain.
500-----	10	..do....	3 died after 1 or 2, 45-percent weight gain in survivors.
Controls.	-----	-----	50-percent weight gain.

¹ Butoxone Amine®, 26.3 percent water soluble concentrate of 2,4-DB, Rhodia, Inc., Chipman Div., New Brunswick, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

Chlorinated Aliphatic Acid Compounds

2-(2,4,5-trichlorophenoxy)ethyl 2,2-dichloropropionate and related compounds (erbon)

All test animals were dosed by capsule (table 11). Two yearlings and two sheep had weight losses at 25 mg./kg., but two other sheep were not affected by this dosage. Chickens had reduced weight gains at 175 mg./kg., with weight loss or death occurring at higher dosage levels.

A metabolic study of erbon was carried out in conjunction with these trials.⁷

Diarrhea was the initial sign of poisoning in most affected sheep; in other sheep and cattle,

⁷ WRIGHT, F. C., RINER, J. C., and GILBERT, B. N. GAS CHROMATOGRAPHIC DETERMINATION OF ERBON AND TWO METABOLITES IN BIOLOGICAL MATERIALS. Jour. Agr. Food Chem. 17(6): 1171-1173. 1969.

the only sign was anorexia. In one sheep, conjunctivitis and ataxia were evident before death.

At necropsy, involvement of the respiratory and digestive tracts were characterized by congested mucosa. The liver and kidneys were en-

gorged with blood and the spleen and adrenals were often enlarged. Chickens had swollen, congested liver and kidneys and reddened intestinal mucosa.

Application rates for erbon for grass and broadleaf weed control in noncrop areas range from 40 to 160 pounds actual per acre. These rates would be highly hazardous for the three test species.

TABLE 11.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with 2-(2,4,5-trichlorophenoxy)ethyl 2,2-dichloropropionate and related compounds*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
25-----	10	13-percent weight loss.
25-----	10	14-percent weight loss.
50-----	10	21-percent weight loss.
Sheep:		
10-----	10	NIE.
25-----	10	Do.
25-----	10	Do.
25-----	10	Poisoned after 3 and survived, 8-percent weight loss.
25-----	10	23-percent weight loss.
50-----	10	Poisoned after 2 and survived, 7-percent weight loss.
50-----	10	13-percent weight loss.
50-----	7	Poisoned and died.
50-----	7	Do.
50-----	34	Do.
100-----	6	Do.
100-----	7	Poisoned after 5 and died.
100-----	6	Poisoned after 3 and died.
100-----	8	Poisoned after 2 and died.
250-----	4	Poisoned after 2 and died.
500-----	2	Poisoned and died.
Chickens: ³		
25-----	10	51-percent weight gain.
50-----	10	42-percent weight gain.
100-----	10	44-percent weight gain.
175-----	10	32-percent weight gain.
200-----	10	4-percent weight loss.
250-----	10	All died after 8 to 10.
500-----	9	All died after 6 to 9.
Controls-----		44-percent weight gain.

¹ Baron®, 41 percent emulsifiable concentrate of erbon, Dow Chemical Co., Midland, Mich.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

2-[(4-chloro-*o*-tolyl) oxy]propionic acid (mecoprop), diethanolamine salt

Cattle were dosed by capsule, sheep by drench, chickens, by pipette (table 12). One yearling was poisoned after five doses at 175 mg./kg., and one sheep was poisoned after two doses at 250 and died after three doses. Chickens had reduced weight gains at 25 mg./kg. Five chickens died at 250 mg./kg. or higher.

One yearling was affected only by weight loss at 175 mg./kg. Although the appetite was apparently normal during the trial period, the weight loss was due primarily to metabolic interference.

At necropsy on the yearling, the liver and kidneys were congested, the adrenals and spleen were swollen, and petechiae were seen in the subcutaneous tissue. At necropsy on the sheep, the liver and kidneys were congested and the abomasal and intestinal mucosa was reddened. Lesions in chickens were generally limited to engorged liver and swollen, congested kidneys.

Application rates for mecoprop for broadleaf weed control in noncrop areas range from 1 to 1.5 pounds actual per acre. These rates would not be hazardous for cattle and sheep, but a modest increase to 3 pounds per acre would be hazardous for chickens.

trichloroacetic acid (TCA), sodium salt

All test animals were dosed by capsule (table 13). One yearling and one sheep had weight loss at 50 mg./kg., but only one animal for each species was affected by this dosage. A sheep was poisoned after two doses at 175 mg./kg. and a yearling after three doses at 375. Dosages up to and including 500 mg./kg. had no adverse effects on chickens.

The loss of weight resulting from relatively

TABLE 12.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2-[(4-chloro-o-tolyl)oxy]propionic acid, diethanolamine salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
100-----	10	Capsule--	NIE.
100-----	10	..do-----	Do.
175-----	10	..do-----	9-percent weight loss.
175-----	8	..do-----	Poisoned after 5 and survived, 14-percent weight loss.
250-----	2	..do-----	Poisoned and died.
Sheep:			
50-----	10	Drench--	NIE.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
175-----	10	..do-----	Do.
175-----	10	..do-----	Do.
250-----	3	..do-----	Poisoned after 2 and died 4 days after last dose.
Chickens: ³			
10-----	10	Pipette--	40-percent weight gain.
25-----	10	..do-----	20-percent weight gain.
50-----	10	..do-----	27-percent weight gain.
50-----	10	..do-----	31-percent weight gain.
100-----	10	..do-----	29-percent weight gain.
100-----	10	..do-----	Do.
250-----	10	..do-----	1 died after 5, 36-percent weight gain in survivors.
375-----	10	..do-----	2 died after 2 and 4, 34-percent weight gain in survivors.
500-----	10	..do-----	2 died after 4 and 9, 26-percent weight gain in survivors.
Controls-----			44-percent weight gain

¹ Chipco Turf Herbicide®, 32.8 percent water soluble concentrate of mecoprop, Rhodia Inc., Chipman Div., New Brunswick, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

low dosage levels in the two affected test animals was due to metabolic interference because

TABLE 13.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with trichloroacetic acid (TCA), sodium salt*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
25-----	10	NIE.
50-----	10	Do.
50-----	10	6-percent weight loss.
100-----	10	NIE.
175-----	10	Do.
250-----	10	Do.
375-----	7	Poisoned after 3 and survived, 6-percent weight loss.
Sheep:		
25-----	10	NIE.
50-----	10	13-percent weight loss.
100-----	10	NIE.
100-----	10	Do.
175-----	10	Poisoned after 2 and survived, 11-percent weight loss.
250-----	2	Poisoned and survived, 12-percent weight loss.
Chickens: ³		
100-----	10	47-percent weight gain.
250-----	10	Do.
500-----	10	51-percent weight gain.
Controls-----		50-percent weight gain.

¹ Sodium TCA Grass Killer®, 95 percent pellets, Dow Chemical Co., Midland, Mich.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

the appetites were not impaired. The poisoned yearling had severe diarrhea and ataxia. The sheep dosed at 175 mg./kg. had anorexia, whereas the sheep dosed at the higher rates had anorexia and depression before prostration.

Application rates for TCA range from 3.3 to 45 pounds actual per acre. Rates in excess of 25 pounds would be hazardous for sheep, and the maximum rate would be hazardous for cattle. Chickens should not be adversely affected by these rates.

Amide Compounds

***O,O*-diisopropyl phosphorodithioate S-ester with *N*-(2-mercaptoethyl) benzenesulfonamide (bensulide)**

All test animals were dosed by capsule (table 14). One yearling was poisoned after two doses at 50 mg./kg. and one sheep after three doses at 100. Chickens had reduced weight gains at 50 mg./kg.

The only sign of poisoning in sheep was anorexia, but salivation, diarrhea, prostration, and ataxia also were seen in cattle.

At necropsy, there were congested lungs and redness of the upper respiratory mucosa in both sheep. In one sheep the only other lesion was a reddened pancreas, and in the other there were engorged kidneys and congested intestinal mucosa. Chickens had swollen liver and reddened intestinal mucosa.

Application rates for bensulide range from 2 to 6 pounds actual per acre. The maximum rate would be hazardous for cattle and chickens, but not for sheep.

2,6-dichlorothiobenzamide (chlor- thiamid)

All test animals were dosed by capsule. One yearling was poisoned after five doses at 10 mg./kg., and one sheep had weight loss at 25 (table 15). One group of chickens had reduced weight gains at 5 mg./kg., but that dosage had no adverse effects on another group.

Poisoned cattle had various degrees of anorexia, with accompanying depression and weakness. Similarly, the sheep that survived the 50-mg./kg. regimen had almost complete anorexia after being initially affected. The other two affected sheep had no observable signs before the completion of the trial or until the death of one was imminent.

At necropsy, the sheep had congested liver and kidneys, distended cranial vessels, and swollen lymph nodes related to reddened intestinal

TABLE 14.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with O, O-diisopropyl phosphorodithioate S-ester with N-(2-mercaptoethyl) benzenesulfonamide*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
25-----	10	NIE.
25-----	10	Do.
50-----	10	Do.
50-----	2	Poisoned and survived.
100-----	2	Poisoned and survived, 9-percent weight loss.
Sheep:		
50-----	10	NIE.
50-----	10	Do.
100-----	8	Poisoned after 5 and died.
100-----	3	Poisoned and died.
Chickens: ³		
25-----	10	51-percent weight gain.
50-----	10	31-percent weight gain.
100-----	10	30-percent weight gain.
250-----	10	1-percent weight gain.
375-----	10	3 died after 8 to 10, 36-percent weight loss in survivors.
500-----	10	2 died after 5 and 7, 34-percent weight loss in survivors.
Controls----	-----	44-percent weight gain.

¹ Betesan 4-E®, 45.2 percent emulsifiable concentrate of bensulide, Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

mucosa. The chicken had a congested intestinal tract.

There is no current registration for chlor-thiamid in agriculture. An application rate of 1 pound actual per acre would be hazardous for cattle and chickens. A 3-pound-rate equivalent would be hazardous for sheep.

Phenyl Urea Compounds

3-(hexahydro-4,7-methanoindan-5-yl)-1,1-dimethylurea (norea)

Cattle and sheep were dosed by capsule or drench, chickens by capsule (table 16). A yearling was poisoned after two doses at 175 mg./kg. and a sheep after five doses at 250. A greater dosage (500 mg./kg.) had no adverse effects on chickens.

TABLE 15.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with 2,6-dichlorothiobenzamide¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
5-----	10	NIE.
5-----	10	Do.
10-----	10	Do.
10-----	10	Poisoned after 2 and survived, 6-percent weight loss.
25-----	7	Poisoned after 2 and survived, 11-percent weight loss.
25-----	6	Poisoned after 3 and survived, 20-percent weight loss.
Sheep:		
10-----	10	NIE.
10-----	10	Do.
25-----	10	Do.
25-----	10	13-percent weight loss.
50-----	10	Poisoned after 1 and survived, 26-percent weight loss.
50-----	2	Poisoned and died.
Chickens: ³		
5-----	10	49-percent weight gain.
5-----	10	36-percent weight gain.
10-----	10	43-percent weight gain.
10-----	10	36-percent weight gain.
25-----	10	28-percent weight gain.
50-----	10	15-percent weight gain.
100-----	10	1 died after 10, 6-percent weight loss in survivors.
Controls-----		48-percent weight gain.

¹ Prefix®, 7.5 percent granules of chlorthiamid, Shell Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

An enlargement, developed in the mandibular area of the drenched yearling, gave evidence of the irritating effects of this chemical on the mucous membrane. It was not considered a part of norea toxicity to cattle. Other cattle had ataxia, vomition (forceful expulsion) of rumen contents, anorexia, and diarrhea. One yearling developed acute urticarial lesions in the cervical area. These smooth, slightly elevated, skin erup-

TABLE 16.—Results of multiple oral dosing of cattle, sheep, and chickens with 3-(hexahydro-4,7-methanoindan-5-yl)-1,1-dimethylurea¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
100-----	10	Capsule--	NIE.
100-----	10	--do-----	Do.
175-----	10	--do-----	Do.
175-----	9	--do-----	Poisoned after 2 and survived, 18-percent weight loss.
250-----	1	--do-----	Poisoned and survived.
250-----	2	Drench--	Poisoned and survived, 7-percent weight loss. ³
Sheep:			
50-----	10	Capsule--	NIE.
100-----	10	--do-----	Do.
100-----	10	--do-----	Do.
175-----	10	--do-----	Do.
175-----	10	--do-----	Do.
250-----	10	--do-----	Do.
250-----	9	Drench--	Poisoned after 5 and survived, 19-percent weight loss.
Chickens: ⁴			
250-----	10	Capsule--	49-percent weight gain.
500-----	10	--do-----	55-percent weight gain.
Controls-----			50-percent weight gain.

¹ Herban®, 80 percent wettable powder of norea, Hercules, Inc., Wilmington, Del.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

tions disappeared soon after dosing was discontinued. The poisoned sheep had only anorexia.

Application rates for norea range from 1.8 to 3.2 pounds actual per acre. These rates would not be hazardous for the three test species.

3-[*p*-(*p*-chlorophenoxy)phenyl]-1,1-dimethylurea (chloroxuron)

Cattle and chickens were dosed by capsule, sheep by capsule or drench (table 17). One yearling was poisoned after five doses at 25 mg./kg. and a sheep after eight doses. Chickens had reduced weight gains at 50 mg./kg.

The onset of poisoning in test animals was

TABLE 17.—*Results of multiple oral dosing of cattle, sheep, and chickens with 3-[p-(p-chlorophenoxy)phenyl]-1,1-dimethylurea*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
10-----	10	Capsule--	NIE.
10-----	10	do-----	Do.
25-----	10	do-----	Do.
25-----	5	do-----	Poisoned and died.
50-----	10	do-----	NIE.
50-----	2	do-----	Poisoned and survived.
100-----	1	do-----	Do.
Sheep:			
10-----	10	do-----	NIE.
10-----	10	do-----	Do.
25-----	10	do-----	Do.
25-----	8	do-----	Poisoned and survived.
50-----	10	do-----	8-percent weight loss.
50-----	3	do-----	Poisoned and survived.
100-----	2	Drench--	Poisoned and died.
Chickens: ³			
10-----	10	Capsule--	64-percent weight gain.
25-----	10	do-----	59-percent weight gain.
50-----	10	do-----	51-percent weight gain.
100-----	10	do-----	1-percent weight gain.
250-----	6	do-----	All died after 4 to 6.
500-----	6	do-----	Do.
Controls--			61-percent weight gain.

¹ Tenoran®, 50 percent wettable powder of chloroxuron, Ciba Agrochemical Co., Ciba Corp., Summit, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

usually severe and without preliminary signs. The sudden appearance of ataxia and prostration was followed by anorexia, dyspnea, and depression. Cessation of further dosing usually resulted in survival and complete recovery.

At necropsy, lesions in the yearling and the sheep were reddened abomasal and intestinal mucosa and congestion of the pancreas and kidneys. The cranial vessels were distended and prominent. Lesions in the chickens were congestion of the intestinal mucosa, enlarged light-brown liver, and swollen kidneys.

Application rates for chloroxuron range from 3 to 4 pounds actual per acre. These rates would be hazardous for cattle and sheep, but not for chickens.

1,1-dimethyl-3-(*a,a,a*-trifluoro-*m*-tolyl)urea (fluometuron)

All test animals were dosed by capsule except one sheep, which was dosed by drench (table 18). One yearling was poisoned after two doses at 100 mg./kg. and one sheep after six doses at 50. Chickens had reduced weight gains at 50 mg./kg.

Poisoning in its mildest form was shown in test animals by anorexia and diarrhea. Acute poisoning was shown in sheep by the sudden appearance of ataxia, depression, and anorexia, followed by death within 24 hours from onset. Chickens were depressed, with weight loss at the highest dosage level.

At necropsy, the sheep had reddened abomasal and intestinal mucosa; swollen, edemic lymph nodes; friable, light-brown liver; congested kidneys; and distended cranial vessels.

Application rates for fluometuron for cotton range from 1 to 2 pounds actual per acre. These rates would not be hazardous for the three test species.

3-(*p*-bromophenyl)-1-methoxy-1-methylurea (metobromuron)

All test animals were dosed by capsule (table 19). Chickens were the most susceptible species and had reduced weight gains at 25 mg./kg. One yearling had weight loss at 50 mg./kg., one sheep was poisoned after two doses at 100, and another sheep after five doses at 100.

TABLE 18.—*Results of multiple oral dosing of cattle, sheep, and chickens with 1,1-dimethyl-3-(a,a,a-trifluoro-m-tolyl)urea*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	Number		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	do-----	Do.
100-----	10	do-----	7-percent weight loss.
100-----	10	do-----	Poisoned 2 and survived, 15-percent weight loss.
Sheep:			
25-----	10	do-----	NIE.
25-----	10	do-----	Do.
50-----	10	do-----	Do.
50-----	10	do-----	Poisoned after 6 and survived, 5-percent weight loss.
100-----	10	do-----	NIE.
100-----	10	do-----	Poisoned after 3 and survived, 8-percent weight loss.
175-----	2	do-----	Poisoned and died.
250-----	2	Drench--	Do.
Chickens: ³			
25-----	10	Capsule--	65-percent weight gain.
50-----	10	do-----	54-percent weight gain.
100-----	10	do-----	47-percent weight gain.
250-----	10	do-----	35-percent weight gain.
500-----	10	do-----	8-percent weight loss.
Controls--			61-percent weight gain.

TABLE 19.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with 3-(p-bromophenyl)-1-methoxy-1-methylurea*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
25-----	10	NIE.
25-----	10	Do.
25-----	10	Do.
50-----	10	5-percent weight loss.
50-----	10	Do.
100-----	10	Poisoned after 7 and survived, 12-percent weight loss.
Sheep:		
50-----	10	NIE.
50-----	10	Do.
100-----	10	Poisoned after 5 and survived, 17-percent weight loss.
100-----	4	Poisoned after 2 and survived, 8-percent weight loss.
Chickens: ³		
10-----	10	76-percent weight gain.
25-----	10	51-percent weight gain.
50-----	10	32-percent weight gain.
100-----	10	35-percent weight loss.
250-----	6	All died after 4 to 6.
500-----	4	All died after 2 to 4.
Controls--		61-percent weight gain.

¹ Patoran®, 50 percent wettable powder of metobromuron, Ciba Agrochemical Co., Ciba Corp., Summit, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

¹ Cotoran®, 80 percent wettable powder of fluometuron, Ciba Agrochemical Co., Ciba Corp., Summit, N.J.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

Signs of poisoning were absent in cattle having weight losses at 50 mg./kg., indicating probable metabolic interference. The one yearling and one of the sheep dosed at 100 mg./kg. had anorexia only. The other sheep dosed at 100 had severe depression and hematuria (blood

in urine). However, there were no deaths in these animals.

Chickens were depressed before death and at necropsy had swollen liver and kidneys and congested intestinal mucosa.

The application rate for metobromuron for potatoes is 3 pounds actual per acre. This rate would be hazardous for chickens, but not for cattle or sheep.

Carbamate Compounds

3,4-dichlorobenzyl methylcarbamate (dichlormate)

All test animals were dosed by capsule (table 20). One yearling had weight loss at 10 mg./kg., but another was not affected at 50. A similar observation was made with sheep at either 50 or 100 mg./kg. Chickens had reduced weight gains at 175 mg./kg.

Cattle and sheep dosed at 50 mg./kg. or lower had no observable signs of poisoning, but weight losses of 5 to 9 percent were recorded during the trial periods. Similarly, a sheep dosed at 100 mg./kg. had no observable signs, but weight losses of 10 percent were recorded; however, there was a delayed alopecic effect (loss of hair or wool—either partial or complete) beginning 2 days after the last dose. Other sheep dosed at higher rates had anorexia and diarrhea, and cattle had anorexia, diarrhea, tympanites (distended with gas), and ataxia.

At necropsy on the yearling, the upper respiratory system and abomasal and intestinal mucosa were congested; mesenteric lymph nodes were swollen; there were hemorrhages on the epicardium, on the kidney cortex, and in the subcutaneous tissue; the liver was enlarged; and the gall bladder was distended. Chickens had congested liver, swollen, edematous kidneys, and reddened intestinal mucosa.

There are no current registrations for dichlormate. An application rate of 1 pound actual per acre would be hazardous for cattle, but not sheep or chickens.

isopropyl *m*-chlorocarbanilate (chlorpropham)

Cattle and sheep were dosed by capsule or drench, chickens by capsule (table 21). Three of four yearlings had weight losses at 100 mg./kg., with two poisoned after two and five doses. One of three sheep had a weight loss at 100 mg./kg., but the other two, in addition to

two sheep at 175, were not affected. All species were adversely affected after two to 10 doses at 100 mg./kg., but larger dosages had no greater

TABLE 20.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with 3,4-dichlorobenzyl methylcarbamate*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
5-----	10	NIE.
10-----	10	Do.
10-----	10	5-percent weight loss.
25-----	10	8-percent weight loss.
50-----	10	NIE.
50-----	10	9-percent weight loss.
100-----	4	Poisoned after 3 and survived, 8-percent weight loss.
250-----	2	Poisoned and died.
Sheep:		
25-----	10	NIE.
50-----	10	Do.
50-----	10	Do.
50-----	10	7-percent weight loss.
100-----	10	NIE.
100-----	10	10-percent weight loss, delayed alopecia.
100-----	10	Poisoned after 2 and survived, 7-percent weight loss.
250-----	10	Poisoned after 2 and survived, 17-percent weight loss.
Chickens: ³		
100-----	10	63-percent weight gain.
175-----	10	38-percent weight gain.
250-----	10	22-percent weight gain.
375-----	10	2 died after 7 and 10, 15-percent weight gain in survivors.
500-----	6	All died after 2 to 6.
Controls----	-----	55-percent weight gain.

¹ Rowmate 4E®, 45 percent emulsifiable concentrate of dichlormate, Hercules, Inc., Wilmington, Del.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

effect on weight gains of chickens than the 100-mg./kg. dosage had.

The only sign of poisoning was anorexia, except for the sheep that was acutely poisoned and died. No forewarning signs were observed in this animal. One yearling developed a mandibular enlargement following two consecutive drenches. This enlargement was considered to be due to chemical irritation of the pharyngeal

mucosa. It was not considered part of chlorpropham toxicity to cattle.

At necropsy, the sheep had congested lungs, liver, and kidneys. The spleen was swollen and its contents were brownish red.

Application rates for chlorpropham range from 2 to 20 pounds actual per acre. Rates of 12 pounds or more would be hazardous for all three test species.

Thiocarbamate Compounds

S-propyl butylethylthiocarbamate (pebulate)

All test animals were dosed by capsule (table 22). A yearling was poisoned after one dose at 50 mg./kg. and a sheep after three doses at 175. Chickens had reduced weight gains at 100 mg./kg.

Anorexia was the initial sign of poisoning. As additional doses were given to cattle and sheep, first there were diarrhea and increased salivation, then usually depression and prostration. Ataxia was seen occasionally in poisoned cattle and either tympanites or dyspnea in poisoned sheep.

At necropsy on cattle and sheep, there were hemorrhages in the subcutaneous tissue and muscles, congested lungs and thyroid, and reddened gastrointestinal mucosa. The liver was enlarged and friable and the kidneys were engorged with blood. Chickens had swollen kidneys with a yellowish cast, reddened intestinal mucosa, and enlarged liver.

Application rates for pebulate range from 4 to 6 pounds actual per acre. The maximum rate would be hazardous for cattle, but not for sheep or chickens.

S-propyl dipropylthiocarbamate (vernolate)

All animals were dosed by capsule except two sheep, which were dosed by drench (table 23). Two yearlings were poisoned after three and four doses at 100 mg./kg. Two of four sheep died after eight and 10 doses at 250 mg./kg., but the other two were not affected by this dosage. Chickens had reduced weight gains at 100 mg./kg.

Anorexia was the most general sign of poisoning in cattle and sheep; however, weakness, muscular spasms, and ataxia were delayed effects in one of the yearlings.

At necropsy, the liver was light brown, the lungs were usually blood engorged, the respiratory mucosa was reddened, and the tract was filled with froth. There were 2 to 4 liters of excess fluid in the abdominal and thoracic cavities. The thyroid and the intestinal mucosa were congested. The adrenals were swollen in one sheep.

Application rates for vernolate range from 2.5 to 3 pounds actual per acre. These rates would not be hazardous for the three test species.

S-ethyl dipropylthiocarbamate (EPTC)

All test animals were dosed by capsule (table 24). Three yearlings were poisoned after one and four doses at 50 mg./kg. Two sheep were poisoned and died after two doses at 100 mg./kg., but another sheep was not affected by this dosage. Chickens had reduced weight gains at 50 mg./kg., but larger dosages had no greater effects on weight gains of chickens than the 50-mg./kg. dosage had.

The severity of poisoning to cattle and sheep could not be forecasted by the signs of poisoning observed. Anorexia, either partial or complete, was the only deviation from normal in all animals except one yearling dosed at 50 mg./kg. In that yearling an ataxic condition developed, associated with prostration and convulsions. Further dosing was discontinued, and the yearling survived.

At necropsy, the most prominent lesion was

TABLE 21.—*Results of multiple oral dosing of cattle, sheep, and chickens with isopropyl m-chlorocarbaniolate*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	--do-----	Do.
100-----	10	--do-----	Do.
100-----	10	--do-----	5-percent weight loss.
100-----	10	Drench--	Poisoned after 5 and survived, 9-percent weight loss.
100-----	10	--do-----	Poisoned after 2 and survived, 9-percent weight loss. ³
Sheep:			
50-----	10	Capsule--	NIE.
100-----	10	--do-----	Do.
100-----	10	Drench--	Do.
100-----	10	Capsule--	9-percent weight loss.
175-----	10	--do-----	NIE.
175-----	10	Drench--	Do.
250-----	5	--do-----	Poisoned and died.
Chickens: ⁴			
50-----	10	Capsule--	69-percent weight gain.
100-----	10	--do-----	52-percent weight gain.
250-----	10	--do-----	58-percent weight gain.
500-----	10	--do-----	56-percent weight gain.
Controls-----			64-percent weight gain.

¹ Chloro IPC®, 47 percent emulsifiable concentrate of chlorpropham, Chemical Div., PPG Industries, Inc., Pittsburgh, Pa.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

an enlarged, light-brown, friable liver. The lungs and upper respiratory tract and the kidneys were congested. There were hemorrhages in the subcutaneous tissue and muscles, and the large intestines were congested, with reddened mucosa.

Application rates for EPTC range from 1.5 to 7.5 pounds per acre. The maximum rate would be hazardous for cattle and chickens, but not for sheep.

TABLE 22.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with S-propyl butylethylthiocarbamate*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
10-----	10	NIE.
25-----	10	Do.
25-----	10	Do.
50-----	1	Poisoned and survived.
100-----	6	Poisoned after 2 and died.
100-----	5	Do.
100-----	3	Poisoned and died.
Sheep:		
50-----	10	NIE.
100-----	10	Do.
100-----	10	Do.
175-----	10	Poisoned after 3 and survived, 8-percent weight loss.
250-----	10	Poisoned after 2 and survived, 9-percent weight loss.
250-----	8	Poisoned after 2 and died.
250-----	8	Do.
250-----	4	Poisoned after 3 and died.
Chickens: ³		
50-----	10	40-percent weight gain.
100-----	10	24-percent weight gain.
250-----	10	16-percent weight gain.
375-----	10	4-percent weight gain.
500-----	10	2 died after 7 and 9, 1-percent weight loss in survivors.
Controls-----		33-percent weight gain.

¹ Tillam 6E®, 76 percent emulsifiable concentrate of pebulate, Agr. Chem. Div., Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

S-ethyl dipropylthiocarbamate (EPTC) and (2,4-dichlorophenoxy) acetic acid (2,4-D), iso-octyl ester

All test animals were dosed by capsule (table 25). One yearling had a weight loss at 25 mg./kg., but another was not affected by this dosage. Two sheep were poisoned after four and five doses at 100 mg./kg., but another was not affected by this dosage. Chickens had reduced weight gains only at 500 mg./kg.

TABLE 23.—*Results of multiple oral dosing of cattle, sheep, and chickens with S-propyl di-propylthiocarbamate*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	--do-----	Do.
100-----	10	--do-----	Poisoned after 4 and survived, 6-percent weight loss, delayed toxicity after 8 days.
100-----	4	--do-----	Poisoned after 3 and died 2 days after last dose.
Sheep:			
100-----	10	--do-----	NIE.
100-----	10	--do-----	Do.
250-----	10	--do-----	Do.
250-----	10	Drench--	Do.
250-----	10	Capsule--	Poisoned and died.
250-----	8	--do-----	Do.
375-----	10	Drench--	NIE.
375-----	6	Capsule--	Poisoned after 3 and died.
Chickens: ³			
25-----	10	--do-----	68-percent weight gain.
50-----	10	--do-----	57-percent weight gain.
100-----	10	--do-----	28-percent weight gain.
250-----	10	--do-----	23-percent weight gain.
500-----	10	--do-----	2-percent weight gain.
Controls--	-----	-----	49-percent weight gain.

¹ Vernam 6E®, 75.9 percent emulsifiable concentrate of vernolate, Agr. Chem. Div., Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

Signs of poisoning were anorexia and diarrhea in cattle and sheep. Depression and prostration preceded death.

At necropsy, the liver was enlarged and friable and the kidneys were congested. The abomasal and intestinal mucosa was reddened and associated with rumen stasis characterized by bright, undigested feed. The sheep had swollen spleen and congested pancreas and thyroid. The yearling had hemorrhages on the epicardium and congested lungs, with blood-tinged froth in the respiratory tract.

TABLE 24.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with S-ethyl dipropylthiocarbamate*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
25-----	10	NIE.
25-----	10	Do.
25-----	10	Do.
50-----	4	Poisoned and survived.
50-----	4	Poisoned after 1 and died.
50-----	3	Do.
100-----	3	Do.
Sheep:		
50-----	10	NIE.
50-----	10	Do.
100-----	10	Do.
100-----	2	Poisoned and died.
100-----	2	Do.
250-----	2	Poisoned after 1 and died.
250-----	1	Poisoned and died.
Chickens: ³		
25-----	10	57-percent weight gain.
50-----	10	32-percent weight gain.
100-----	10	30-percent weight gain.
250-----	10	33-percent weight gain.
500-----	10	29-percent weight gain.
Controls--	-----	52-percent weight gain.

¹ Eptam 6E®, 75.5 percent emulsifiable concentrate of EPTC, Agr. Chem. Div., Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

The application rate for this EPTC and 2,4-D mixture for annual grasses and broadleaf weed control in corn is 2 quarts per acre. This would be the equivalent of 2 pounds of EPTC and 1 pound of 2,4-D per acre. This rate would be hazardous for cattle, but not for sheep and chickens.

2-chloroallyl diethyldithiocarbamate (CDEC)

Cattle were dosed by drench or capsule, sheep by drench, chickens by pipette (table 26). Two yearlings were poisoned after one and three doses at 25 mg./kg., and one sheep was poisoned

TABLE 25.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with S-ethyl dipropylthiocarbamate and (2,4-dichlorophenoxy)acetic acid, iso-octyl ester¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
10-----	10	NIE.
25 ³ -----	10	Do.
25 ³ -----	10	5-percent weight loss.
50-----	10	NIE.
50-----	7	Poisoned after 2 and survived, 5-percent weight loss.
100-----	2	Poisoned after 1 and died.
Sheep:		
50-----	10	NIE.
50-----	10	Do.
50-----	10	Do.
50-----	10	Do.
100-----	10	Do.
100-----	5	Poisoned and died.
100-----	5	Poisoned after 4 and died.
250-----	5	Poisoned and died.
250-----	4	Poisoned after 3 and died.
Chickens: ⁴		
100-----	10	64-percent weight gain.
250-----	10	58-percent weight gain.
500-----	10	39-percent weight gain.
Controls-----		49-percent weight gain.

¹ Knoxweed 42®, 82.8 percent emulsifiable concentrate (46.9 percent EPTC and 35.4 percent 2,4-D), Agr. Chem. Div., Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ 25 mg./kg. is equivalent to 14.25 mg./kg. EPTC and 10.75 mg./kg. 2,4-D.

⁴ Average results of 5 treated chickens.

after three doses at 25. One yearling developed a mandibular swelling after six doses at 10 mg./kg. by drench, but this was not considered a part of CDEC toxicity to cattle. Chickens had reduced weight gains at 100 mg./kg. Although two chickens in one group died and there were weight losses in three survivors at 175 mg./kg., no chickens died and there were slight weight gains in another group at 250.

Interstitial keratitis developed in one of three sheep dosed at 25 mg./kg. and in both sheep at

TABLE 26.—Results of multiple oral dosing of cattle, sheep, and chickens with 2-chloroallyl diethyldithiocarbamate¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	Number		
Cattle:			
10-----	10	Capsule--	NIE.
10-----	10	--do-----	Do.
10-----	10	Drench--	Do.
10-----	10	--do-----	Irritation effect after 6 and survived, 15-percent weight loss. ³
25-----	8	--do-----	Poisoned after 3 and survived, 8-percent weight loss.
25-----	5	--do-----	Poisoned after 1 and sacrificed 5 days after last dose.
Sheep:			
10-----	10	--do-----	NIE.
10-----	10	--do-----	Do.
25-----	10	--do-----	Do.
25-----	10	--do-----	15-percent weight loss.
25-----	3	--do-----	Poisoned and survived. ⁴
50-----	4	--do-----	Poisoned after 1 and survived, 6-percent weight loss. ⁴
50-----	7	--do-----	Poisoned and survived, 5-percent weight loss. ⁴
Chickens: ⁵			
50-----	10	Pipette--	56-percent weight gain.
100-----	10	--do-----	46-percent weight gain.
175-----	10	--do-----	2 died after 7, 6-percent weight loss in survivors.
250-----	10	--do-----	13-percent weight gain.
Controls-----			51-percent weight gain.

¹ Vegadex®, 46.4 percent emulsifiable concentrate of CDEC, Monsanto Co., St. Louis, Mo.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Bilateral, interstitial keratitis.

⁵ Average results of 5 treated chickens.

50. Both eyes of each affected sheep were involved, with opaqueness of the cornea and conjunctivitis, associated with pain, photophobia, and lacrimation. This condition was corrected

with appropriate therapy. All made a complete recovery except one sheep (poisoned after one dose at 50 mg./kg.) that developed a partial alopecic condition with loss of wool. Other signs of poisoning shown in these and other sheep and cattle were anorexia, dyspnea, ataxia, and salivation. However, one sheep with 15-percent weight loss at 25 mg./kg. appeared normal throughout the trial.

At necropsy, the yearling that was chronically

affected and sacrificed had a light-brown, friable liver and excessive quantities of clear fluid in the subcutaneous tissue, joints, and abdominal and thoracic cavities. The two chickens had congested liver and kidneys and reddened intestinal mucosa.

Application rates for CDEC range from 3 to 8 pounds actual per acre. These rates would be hazardous for cattle and sheep, but not for chickens.

Arsenical Compounds

monosodium methanearsonate (MSMA)

All test animals were dosed by capsule (table 27). A yearling was poisoned after two doses at 10 mg./kg. Two sheep were poisoned after

TABLE 27.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with monosodium methanearsonate*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
5-----	10	NIE.
5-----	10	Do.
10-----	5	Poisoned after 2 and died.
25-----	7	Do.
50-----	4	Do.
Sheep:		
25-----	10	NIE.
25-----	10	Do.
50-----	10	Do.
50-----	6	Poisoned after 4 and died.
50-----	7	Poisoned after 3 and survived, 18-percent weight loss.
100-----	2	Poisoned and died.
Chickens: ³		
25-----	10	62-percent weight gain.
50-----	10	60-percent weight gain.
100-----	10	57-percent weight gain.
250-----	10	53-percent weight gain.
Controls-----		64-percent weight gain.

¹ Ansar 170®, 51.3 percent emulsifiable concentrate of MSMA, The Ansul Co., Marinette, Wis.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

three and four doses at 50 mg./kg., but another was not affected by this dosage. Chickens had reduced weight gains at 100 mg./kg. or greater.

Signs of poisoning in cattle and sheep were anorexia, hematuria, diarrhea, and depression.

At necropsy, the most notable lesions involved the gastrointestinal tract in which the mucosa of the rumen, abomasum, and intestines was hemorrhagic, with distended and prominent vessels. The liver and kidneys were usually congested, the spleen bulged, and there were excessive quantities of edematous fluid in the abdominal cavities. In two animals, the liver appeared pale and friable.

The application rate for MSMA for cotton is 2 pounds actual per acre. This rate would be hazardous for cattle, but not for sheep and chickens.

disodium methanearsonate (DSMA)

All test animals were dosed by capsule (table 28). A yearling was poisoned after two doses at 25 mg./kg., and two sheep were poisoned after five doses. Chickens had reduced weight gains at 375 and 500 mg./kg.

The initial sign of poisoning was anorexia, either partial or complete. Subsequently, diarrhea and depression were seen. The sheep that was poisoned and survived had a prolonged recovery period.

At necropsy, the yearling and the sheep had hemorrhagic mucosa of the abomasum and intestines and swollen, edemic mesenteric lymph nodes. The kidneys were congested and petechiae were on the cortex surface. The sheep had excessive edematous fluid in the abdominal

TABLE 28.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with disodium methanearsonate¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
25-----	6	Poisoned after 2 and died 3 days after last dose.
Sheep:		
10-----	10	NIE.
10-----	10	Do.
25-----	6	Poisoned after 5 and died.
25-----	5	Poisoned and survived.
Chickens: ³		
25-----	10	67-percent weight gain.
50-----	10	62-percent weight gain.
100-----	10	55-percent weight gain.
250-----	10	64-percent weight gain.
375-----	10	47-percent weight gain.
500-----	10	40-percent weight gain.
Controls-----		59-percent weight gain.

¹ Ansar 184®, 63 percent wettable powder of DSMA, The Ansul Co., Marinette, Wis.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

cavity and in the distended pericardial sac. The yearling had swollen, bright-orange adrenals.

The application rate for DSMA for cotton is 3 pounds actual per acre. This rate would be hazardous for cattle and sheep, but not for chickens.

hydroxydimethylarsine oxide (cacodylic) acid

Cattle and sheep were dosed by capsule or drench, chickens by pipette (table 29). One yearling was poisoned after eight doses at 25 mg./kg., and one sheep had weight loss after 10 doses at 25; but three other yearlings and four other sheep were not affected by this dosage. A yearling dosed by drench developed a mandibular enlargement after two doses at 10 mg./kg., but this was not considered a part of the toxicity of this herbicide to cattle. One

TABLE 29.—Results of multiple oral dosing of cattle, sheep, and chickens with hydroxydimethylarsine oxide acid¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
5-----	10	Capsule--	NIE.
10-----	10	..do-----	Do.
10-----	10	Drench--	Irritation effect after 2, 5-percent weight loss. ³
25-----	10	..do-----	NIE.
25-----	10	Capsule--	Do.
25-----	10	..do-----	Do.
25-----	10	Drench--	Poisoned after 8 and survived, 5-percent weight loss.
50-----	7	..do-----	Poisoned after 1 and died 4 days after last dose.
Sheep:			
10-----	10	..do-----	NIE.
25-----	10	..do-----	Do.
25-----	10	Capsule--	Do.
25-----	10	..do-----	Do.
25-----	10	..do-----	Do.
25-----	10	..do-----	14-percent weight loss
50-----	10	..do-----	Poisoned after 3 and survived, 21-percent weight loss.
50-----	10	..do-----	Poisoned after 2 and survived, 22-percent weight loss.
Chickens: ⁴			
50-----	10	Pipette--	55-percent weight gain.
100-----	10	..do-----	63-percent weight gain.
100-----	10	..do-----	42-percent weight gain.
175-----	10	..do-----	33-percent weight gain.
250-----	10	..do-----	36-percent weight gain.
500-----	10	..do-----	13-percent weight gain.
Controls-----			53-percent weight gain.

¹ Phytar 560®, 26.5 percent emulsifiable concentrate of hydroxydimethylarsine oxide (cacodylic) acid with 12.7 percent total arsenic, The Ansul Co., Marinette, Wis.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

group of chickens had reduced weight gains at 100 mg./kg., but that dosage had no adverse effects on another group.

Signs of poisoning were anorexia and diarrhea in all animals except the sheep dosed at 25 mg./kg. No abnormal behavior was observed in that sheep during the course of the trial, but a 10-percent weight loss occurred.

At necropsy, the yearling had hemorrhagic mucosa of the abomasum and intestines, with distended vessels, an enlarged, congested liver,

swollen kidneys, and reddened mucosa of the bladder. The spleen was irregular in shape and thickened.

Application rates for this cacodylic acid for noncrop areas range from 7.7 to 8.4 pounds actual per acre. These rates would be hazardous for cattle and sheep, but not for chickens.

Substituted Dinitroaniline Compounds

a,a,a-trifluoro-2,6-dinitro-*N,N*-dipropyl-*p*-toluidine (trifluralin)

All test animals were dosed by capsule (table 30). A yearling and a sheep were poisoned after

TABLE 30.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with a,a,a-trifluoro-2,6-dinitro-N, N-dipropyl-p-toluidine*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
100-----	10	NIE.
100-----	10	Do.
175-----	10	Poisoned after 2 and survived, 9-percent weight loss.
Sheep:		
25-----	10	NIE.
50-----	10	Do.
100-----	10	Do.
100-----	10	Do.
175-----	10	Poisoned after 4 and survived, 17-percent weight loss.
175-----	10	Poisoned after 2 and survived, 20-percent weight loss.
Chickens: ³		
50-----	10	55-percent weight gain.
100-----	10	55-percent weight gain.
250-----	10	48-percent weight gain.
500-----	10	25-percent weight gain.
Controls-----	-----	55-percent weight gain.

¹ Treflan®, 44.5 emulsifiable concentrate of trifluralin, Elanco Products Co., Div. of Eli Lilly and Co., Indianapolis, Ind.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

two doses at 175 mg./kg. and another sheep after four doses. Chickens had reduced weight gains at 250 mg./kg.

Signs of poisoning in cattle and sheep were anorexia and diarrhea. With the termination of the trials, a prolonged recovery period of approximately 1 month followed before the affected animals had regained their original body weight. During this period, the signs of poisoning continued, but gradually decreased in severity.

Application rates for trifluralin range from 0.5 to 2 pounds actual per acre. These rates would not be hazardous for the three test species.

N-butyl-*N*-ethyl-*a,a,a*-trifluoro-2,6-dinitro-*p*-toluidine (benefin)

All test animals were dosed by capsule (table 31). One yearling was poisoned after six doses at 25 mg./kg., but another was not affected by this dosage. Two other yearlings similarly were not affected at 50 mg./kg., indicating possible increased individual susceptibility at the lower level. One sheep was poisoned after two doses at 50 mg./kg. and died, and another had weight loss at 50. Chickens had reduced weight gains at 50 mg./kg. One died after nine doses at 250 mg./kg.

The usual sign of poisoning in cattle and sheep was anorexia; however, tympanites, depression, and prostration also were seen in the two sheep before death.

At necropsy, involvement of the gastrointestinal tract was paramount, with congested mucosa of the abomasum and intestines. The vessels to these affected areas were distended

TABLE 31.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with N-butyl-N-ethyl-a,a,a-trifluoro-2,6-dinitro-p-toluidine*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
25-----	10	Do.
25-----	10	Poisoned after 6 and survived, 5-percent weight loss.
50-----	10	NIE.
50-----	10	Do.
100-----	10	Poisoned after 2 and survived, 11-percent weight loss.
Sheep:		
25-----	10	NIE.
25-----	10	Do.
50-----	10	9-percent weight loss.
50-----	4	Poisoned after 2 and died.
100-----	10	Poisoned after 2 and survived, 26-percent weight loss, sacrificed.
Chickens: ³		
25-----	10	57-percent weight gain.
50-----	10	51-percent weight gain.
100-----	10	44-percent weight gain.
175-----	10	52-percent weight gain.
175-----	10	50-percent weight gain.
250-----	10	1 died after 9, 39-percent weight gain in survivors.
Controls-----		56-percent weight gain.

¹ Balan®, 19.4 percent emulsifiable concentrate of benefin, Elanco Products Co., Div. of Eli Lilly Co., Indianapolis, Ind.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

and the lymph nodes were swollen. The liver was enlarged and friable. The chicken had swollen, edematous kidneys and redness of the mucosa of the small intestine.

The application rate for benefin is 1.5 pounds actual per acre. This rate would not be hazardous for the three test species, but a modest increase to 3 pounds actual per acre would be hazardous for cattle.

4-(methylsulfonyl)-2,6-dinitro-N-N-dipropylaniline (nitralin)

Cattle and sheep were dosed by capsule, chickens by pipette (table 32). A yearling was poisoned after two doses at 250 mg./kg., and a sheep died after two doses at 375. Dosages of 500 mg./kg. had no adverse effects on chickens.

The poisoned yearling initially had vomition of the rumen contents, associated with depression within 2 hours after dosing, but con-

TABLE 32.—*Results of multiple oral dosing of cattle, sheep, and chickens with 4-(methylsulfonyl)-2,6-dinitro-N,N-dipropylaniline*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	Number		
Cattle:			
175-----	10	Capsule--	NIE.
175 ³ -----	10	..do-----	Do.
250-----	10	..do-----	Poisoned after 2 and survived, 13-percent weight loss, died 7 days after last dose.
Sheep:			
50-----	10	..do-----	NIE.
100-----	10	..do-----	Do.
175-----	10	..do-----	Do.
250-----	10	..do-----	Do.
375-----	2	..do-----	Poisoned and died after 2.
500-----	10	..do-----	Poisoned after 4 and survived, 8-percent weight loss.
Chickens: ⁴			
100-----	10	Pipette--	51-percent weight gain.
250-----	10	..do-----	50-percent weight gain.
500-----	10	..do-----	50-percent weight gain.
Controls-----			54-percent weight gain.

¹ Planavin 75®, 75 percent wettable powder of nitralin, Agr. Chem. Div., Shell Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Planavin Herbicide WDL®, 43.6 percent emulsifiable concentrate of nitralin, Shell Chemical Co., used to supplement doses.

See, U.S. DEPARTMENT OF AGRICULTURE. U.S.D.A. SUMMARY OF REGISTERED AGRICULTURAL PESTICIDE CHEMICAL USES. HERBICIDES, DEFOLIANTS, DESSICANTS, PLANT REGULATORS. Ed. 3, v. 1, 227 pp. [Includes replacement pages to Jan. 16, 1970.] 1968.

⁴ Average results of 5 treated chickens.

tinued to consume feed. Following the sixth dose, anorexia was seen and continued until the 10-day regimen was completed. An increasing degree of depression and weakness terminated in death. Signs of poisoning in sheep were weakness, tympanites, increased respiration, and a staggering gait.

At necropsy, the mucosa of the abomasum and intestines was reddened and associated lymph

nodes were swollen and blood engorged; the kidneys were congested; the liver was enlarged; and a distended gall bladder was filled with thick, yellow bile.

Application rates for nitratin range from 1.25 to 1.5 pounds actual per acre. These rates would not be hazardous for the three test species.

Dipyridyl Compounds

1,1'-dimethyl-4,4'-bipyridium ion (paraquat), methylsulfate salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 33). A yearling and a sheep had weight losses at 10 mg./kg. Chickens had reduced weight gains at 25 mg./kg., and one died after nine doses. No lesser dosage was tried. One group of chickens at 100 mg./kg. made gains comparable with those of the controls.

From single oral doses of paraquat to cattle and sheep in another study, the toxicity (expressed as LD₅₀) was reported between 50 and 75 mg./kg.⁸ Our trials indicated death caused by 25 mg./kg. to cattle and sheep after six and seven doses, respectively.

Signs of poisoning in cattle and sheep were anorexia, depression, and diarrhea. Recovery of those poisoned usually was prolonged, extending to 2 months after the trials were terminated. Deaths occurred unexpectedly, with no increase in severity of signs.

At necropsy, hemorrhages were seen in and on the heart and in the thyroid and adrenals. The lungs, liver, and kidneys were usually congested. The cranial and mesenteric vessels were distended and prominent, and swollen, edemic lymph nodes were associated with reddened intestinal mucosa. One sheep had a notable bulged spleen with darkened contents. Lesions in chickens were congested kidneys and liver,

distended gall bladder, and reddened intestinal mucosa.

Application rates for this paraquat salt range from 0.25 to 1 pound actual per acre. The maximum would be hazardous for cattle and sheep, but not for chickens.

6,7-dihydrodipyrido[1,2-a:2',1'-c] pyrazinediium ion (diquat), dibromide salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 34). Two yearlings were poisoned after eight and nine doses at 5 mg./kg., and a sheep was poisoned and died after seven doses at 25. No lesser dosage was tried in cattle. One group of chickens had reduced weight gains at 50 mg./kg., but that dosage had no adverse effects on another group of chickens.

The results from this diquat toxicity study and another study with cattle are comparable. The LD₅₀ from a single oral dose was reported as 30 mg./kg.⁹ From our multiple dosing, one yearling was killed at 5 mg./kg., another by 5 doses at 10.

Signs of poisoning in cattle and sheep were anorexia and depression. Deaths occurred unexpectedly, with no increase in severity of signs after their initial appearance.

At necropsy, the lungs were blood engorged and the respiratory mucosa was reddened. Hemorrhages were seen on the external wall of

⁸ HOWE, D. J. T., and WRIGHT, N. THE TOXICITY OF PARAQUAT AND DIQUAT. New Zealand Weed and Pest Control Conf. Proc. 18(105): 105-114. 1965.

⁹ See footnote 8.

TABLE 33.—*Results of multiple oral dosing of cattle, sheep, and chickens with 1,1'-dimethyl-4,4'-bipyridium ion, methylsulfate salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
5-----	10	Capsule--	NIE.
5-----	10	--do-----	Do.
10-----	10	--do-----	10-percent weight loss, delayed recovery. ³
25-----	6	--do-----	Poisoned after 4 and died.
Sheep:			
5-----	10	--do-----	NIE.
5-----	10	--do-----	Do.
10-----	10	--do-----	10-percent weight loss, delayed recovery. ³
25-----	10	--do-----	NIE.
25-----	7	--do-----	Poisoned after 3 and died.
50-----	10	--do-----	Poisoned after 9 and died.
Chickens: ⁴			
25-----	10	Pipette--	1 died after 9, 47-percent weight gain in survivors.
50-----	10	--do-----	49-percent weight gain.
50-----	10	--do-----	34-percent weight gain.
100-----	10	--do-----	1 died after 8, 30-percent weight gain in survivors.
100-----	10	--do-----	51-percent weight gain.
175-----	10	--do-----	2 died after 6 and 7, 1-percent weight loss in survivors.
250-----	10	--do-----	3-percent weight gain.
500-----	10	--do-----	2 died after 9 and 10, 15-percent weight gain in survivors.
Controls.	-----	-----	54-percent weight gain.

¹ Dual Paraquat®, 42 percent emulsifiable concentrate of paraquat, Ortho Div., Chevron Chemical Co., San Francisco, Calif.

² NIE indicates no ill effects apparent.

³ 6 to 8 weeks before regaining original body weight.

⁴ Average results of 5 treated chickens.

the abomasum, on the cerebellar surface, and in swollen adrenals. The liver was congested, and the intestinal mucosa was hemorrhagic. Chickens had swollen, edemic kidneys, congested liver, and petechiae in the intestinal mucosa.

TABLE 34.—*Results of multiple oral dosing of cattle, sheep, and chickens with 6,7-dihydrodipyrido[1,2-a:2',1'-c]pyrazinediium ion, dibromide salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
5-----	10	Capsule--	Poisoned after 9, 5-percent weight loss.
5-----	10	--do-----	Poisoned after 8, 8-percent weight loss, died 2 days after last dose.
10-----	5	--do-----	Poisoned after 2 and died.
25-----	3	--do-----	Poisoned and died.
Sheep:			
10-----	10	--do-----	NIE.
10-----	10	--do-----	Do.
25-----	10	--do-----	Do.
25-----	7	--do-----	Poisoned after 3 and died.
50-----	4	--do-----	Poisoned after 1 and died.
Chickens: ³			
25-----	10	Pipette--	54-percent weight gain.
50-----	10	--do-----	55-percent weight gain.
50-----	10	--do-----	49-percent weight gain.
100-----	10	--do-----	44-percent weight gain.
100-----	10	--do-----	1 died after 7, 38-percent weight gain in survivors.
175-----	10	--do-----	4 died after 2 to 9, 15-percent weight gain in survivors.
250-----	6	--do-----	All died after 4 to 6.
Controls.	-----	-----	54-percent weight gain.

¹ Diquat Dibromide®, 35.3 percent emulsifiable concentrate of diquat, Ortho Div., Chevron Chemical Co., San Francisco, Calif.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

Application rates for diquat range from 0.47 to 1.88 pounds actual per acre and 3 pounds per acre for floating weeds in canals. Rates in excess of 1 pound would be hazardous for cattle, 3 pounds for sheep. The rates would not be hazardous for chickens.

Phthalamic Acid Compounds

N-1-naphthylphthalamic acid (naptalam), sodium salt

Cattle and sheep were dosed by drench, chickens by pipette (table 35). A yearling was poisoned after six doses at 175 mg./kg. Two sheep were similarly poisoned after three and 10 doses at 100 mg./kg., but three other sheep were not affected by this dosage. One chicken in a group died after one dose at 250 mg./kg., but the survivors made gains comparable with those of the controls.

Signs of poisoning were anorexia and diarrhea in one yearling and one sheep. Two other sheep showed no signs of poisoning in the course of the trial, although one had a 17-percent weight loss at 100 mg./kg. and the other had a 4-percent loss at 175.

The sheep that had a 4-percent loss became prostrated and moribund with complete anorexia within 12 days after the last dose. It was then sacrificed. The sheep that had the 17-percent weight loss had no signs of poisoning for 45 days after the last dose. During the following 3 weeks, it began to lose weight again, but showed only partial anorexia. During this period a loose, edematous enlargement developed under the mandible, and the sheep died.

At necropsy, the sacrificed sheep had a reddened intestinal mucosa and congested kidneys and liver. The sheep that died 67 days after the last dose had clear, edematous fluid in the subcutaneous tissue and pericardial sac. Petechiae were seen on the kidney cortex and unclotted blood in the muscles. Lesions in chickens were congestion of the liver and intestinal mucosa and hemorrhages in the spleen.

Application rates for naptalam sodium salt range from 1.26 to 8 pounds actual per acre. These rates would not be hazardous for the three test species.

N-1-naphthylphthalamic acid (naptalam) and 2-*sec*-butyl-4,6-dinitrophenol (dinoseb)

Cattle and sheep were dosed by capsule or drench, chickens by pipette (table 36). Two

yearlings were poisoned after eight doses at 25 mg./kg. One sheep had weight loss at 25 mg./kg., but another sheep was not affected

TABLE 35.—*Results of multiple oral dosing of cattle, sheep, and chickens with N-1-naphthylphthalamic acid, sodium salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	Number		
Cattle:			
50-----	10	Drench	NIE.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
175-----	10	..do-----	Poisoned after 6 and survived, 5-percent weight loss.
Sheep:			
50-----	10	..do-----	NIE.
50-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Do.
100-----	10	..do-----	Poisoned after 3 and survived, 10-percent weight loss.
100-----	10	..do-----	17-percent weight loss, died 67 days after last dose.
175-----	10	..do-----	NIE during trial (4-percent weight loss), sacrificed 12 days after last dose.
Chickens: ³			
50-----	10	Pipette	51-percent weight gain.
100-----	10	..do-----	45-percent weight gain.
250-----	10	..do-----	1 died after 1 dose, 49-percent weight gain in survivors.
500-----	10	..do-----	2 died after 4 and 5, 43-percent weight gain in survivors.
Controls..	-----	-----	49-percent weight gain.

¹ Alanap®, 23.7 percent emulsifiable concentrate of naptalam, Uniroyal Chem., Div. of Uniroyal, Inc., U.S. Rubber Co., Naugatuck, Conn.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

by this dosage. One chicken died after two doses at 25 mg./kg., and survivors in the same group had reduced weight gains.

Signs of poisoning in cattle and sheep were usually anorexia and lethargy and occasionally tympany. One sheep with weight loss appeared normal throughout the trial.

At necropsy, a light-brown, friable liver and a distended gall bladder were the most prominent lesions. In the sheep acutely poisoned at 100 mg./kg., lung congestion was marked. In

other animals fatally affected after more prolonged dosing, the cranial vessels were prominent and hemorrhages were seen around the pituitary. The yearling had swollen adrenals with a yellowish cast. Lesions in chickens were congested kidneys and hemorrhages in the spleen.

Application rates for this naptalam and dinoseb mixture range from 2.25 to 3 pounds actual per acre. The maximum rate would be hazardous for the three test species.

Miscellaneous Compounds

tris[2-(2,4-dichlorophenoxy) ethyl] phosphite (2,4-DEP)

All test animals were dosed by capsule (table 37). Two yearlings had weight losses at 25 mg./kg. Results from trials with sheep and chickens were highly variable, with weight losses or reduced weight gains at various dosage levels in individual sheep or groups of chickens. Dosages of from 10 to 100 mg./kg. had no adverse effects on some sheep and chickens. Nevertheless, dosages of 10 mg./kg. for sheep and 25 for chickens could be expected to cause some adverse effects.

Anorexia was the only sign of poisoning in cattle and sheep, and in a number of instances even anorexia was not evident.

At necropsy, the lesions in the sheep were general. The lungs, kidneys, and thyroid were congested; the upper respiratory and intestinal mucosa was reddened; and the liver was swollen and friable. Chickens had enlarged kidneys and congested intestinal mucosa.

Application rates for 2,4-DEP range from 3 to 6 pounds actual per acre. These rates would be hazardous for the three test species.

5-amino-4-chloro-2-phenyl-3(2H)-pyridazinone (pyrazon)

Cattle were dosed by capsule or drench, sheep and chickens by capsule (table 38). A yearling and a sheep were poisoned and died after three doses at 100 mg./kg. Another yearling developed a mandibular enlargement after two doses by drench at 50 mg./kg., but this was not con-

sidered a part of pyrazon toxicity to cattle. One sheep had a weight loss at 25 mg./kg. and another at 50, but others were not affected by the same dosages. Chickens had reduced weight gains at 250 mg./kg.

Signs of poisoning in cattle and sheep were lethargy and convulsions. In one yearling, convulsions were acute, occurring some 4 hours after the third dose at 100 mg./kg., and were followed by death. In contrast, the sheep with weight loss at 25 mg./kg. was chronically affected. After the sheep apparently had made a complete recovery, convulsions occurred 90 days after the last dose and were followed by death 11 days later.

At necropsy on the acutely poisoned yearlings and sheep, hemorrhagic intestinal mucosa, congested kidneys, and distended cranial vessels were the most prominent lesions. The yearling also had a light-brown, friable liver. Engorged and prominent cranial vessels were the only lesions in the chronically affected sheep.

Application rates for pyrazon range from 4 to 4.8 pounds actual per acre. These rates would be hazardous for sheep, but not for cattle or chickens.

2,4-dichlorophenyl *p*-nitrophenyl ether (nitrofen)

Cattle and chickens were dosed by capsule, sheep by capsule or drench (table 39). A yearling and a sheep were poisoned after three doses at 100 mg./kg., and chickens had weight losses at 175.

Signs of poisoning were anorexia, diarrhea,

hematuria, and depression, with increasing intensity with continued dosing. The affected yearling was also ataxic, with loss of equilibrium.

TABLE 36.—Results of multiple oral dosing of cattle, sheep, and chickens with N-1-naphthylphthalamic acid and 2-sec-butyl-4,6-dinitrophenol¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
10-----	10	Capsule--	NIE.
10-----	10	..do-----	Do.
25 ³ -----	10	Drench--	Poisoned after 8 and survived, 8-percent weight loss. ⁴
25 ³ -----	8	Capsule--	Poisoned and died.
Sheep:			
10-----	10	..do-----	NIE.
10-----	10	Drench--	Do.
25 ³ -----	10	..do-----	Do.
25 ³ -----	10	..do-----	7-percent weight loss.
50-----	10	..do-----	NIE.
50-----	4	..do-----	Poisoned after 3 and survived, 25-percent weight loss.
50-----	6	..do-----	Poisoned and died.
100-----	2	..do-----	Do.
Chickens: ⁵			
10-----	10	Pipette--	66-percent weight gain.
25-----	10	..do-----	1 died after 2, 46-percent weight gain in survivors.
50-----	10	..do-----	3 died after 1 or 2, 6-percent weight gain in survivors.
100-----	1	..do-----	All died after 1.
Controls-----			51-percent weight gain.

¹ Dyanap®, 31.3 percent emulsifiable concentrate of naptalam (20.8 percent) and dinoseb (10.5 percent), Uniroyal Chem., Div. of Uniroyal, Inc., U.S. Rubber Co., Naugatuck, Conn.

² NIE indicates no ill effects apparent.

³ 25 mg./kg. is equivalent to 16.61 mg./kg. naptalam and 8.39 mg./kg. dinoseb.

⁴ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁵ Average results of 5 treated chickens.

At necropsy, the kidneys were congested and the spleen was irregular and swollen. There were hemorrhages on the external surface of the heart, with clotted blood and edematous

TABLE 37.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with tris[2-(2,4-dichlorophenoxy)ethyl]phosphite¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
25-----	10	5-percent weight loss.
25-----	10	Do.
50-----	10	Poisoned after 2 and survived, 5-percent weight loss.
Sheep:		
5-----	10	NIE.
10-----	10	Do.
10-----	10	9-percent weight loss.
25-----	10	NIE.
25-----	10	Do.
25-----	10	7-percent weight loss.
50-----	10	NIE.
50-----	10	Poisoned after 3 and survived, 5-percent weight loss.
50-----	10	Poisoned after 2 and survived, 8-percent weight loss.
100-----	10	NIE.
100-----	5	Poisoned after 2 and died.
Chickens: ³		
10-----	10	66-percent weight gain.
25-----	10	48-percent weight gain.
25-----	10	43-percent weight gain.
50-----	10	56-percent weight gain.
50-----	10	32-percent weight gain.
100-----	10	54-percent weight gain.
100-----	10	42-percent weight gain.
250-----	10	48-percent weight gain.
250-----	10	36-percent weight gain.
375-----	10	1 died after 8, 44-percent weight gain in survivors.
500-----	10	4 died 2 to 7, 8-percent weight loss in survivor.
Controls-----		58-percent weight gain.

¹ Falone®, 44 percent emulsifiable concentrate of 2,4-DEP, Uniroyal Chem., Div. of Uniroyal, Inc., U.S. Rubber Co., Naugatuck, Conn.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

fluid in the pericardial sac. The upper respiratory tract contained froth and edematous fluid. Chickens had congested liver and kidneys and reddened intestinal mucosa.

Application rates for nitrofen range from 4 to 6 pounds actual per acre. These rates would not be hazardous for the three test species.

dimethyl tetrachloroterephthalate (DCPA)

Cattle and chickens were dosed by capsule, sheep by capsule and drench (table 40). A yearling was poisoned after five doses at 250 mg./kg. Sheep were unaffected by dosages up to and including 500 mg./kg.; however, one sheep had weight loss at 50. The result of this trial should, therefore, be considered as solely due to individual susceptibility. Chickens had reduced weight gains at 250 mg./kg.

Anorexia was the only sign of poisoning in the yearling. The sheep appeared normal during and after the trial in all aspects of behavior.

Application rates for DCPA range from 7.5 to 10.5 pounds actual per acre. These rates would not be hazardous for the three test species.

(2,3,6-trichlorophenyl)acetic acid (fenac), sodium salt

Cattle were dosed by capsule or drench, sheep by drench, chickens by pipette (table 41). Two yearlings were poisoned after one and two doses at 50 mg./kg., and one sheep was poisoned after two doses at 175. Chickens had reduced weight gains at 175 mg./kg., and one of the five died after seven doses.

Signs of poisoning in cattle and sheep were anorexia, diarrhea, dyspnea, and ataxia. One sheep had partial paraplegia (paralysis of the hindquarters) after three doses at 250 mg./kg., with death occurring the following day. Another sheep was poisoned and died suddenly after four doses at the same dosage. A sheep that was poisoned and survived had alopecia 30 days after the last dose.

At necropsy on sheep, the intestinal mucosa was reddened, the liver and kidneys were congested, and the spleen was swollen. In the sheep that was acutely poisoned and died, the res-

TABLE 38.—*Results of multiple oral dosing of cattle, sheep, and chickens with 5-amino-4-chloro-2-phenyl-3(2H)-pyridazinone*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
25-----	10	Capsule--	NIE.
25-----	10	--do-----	Do.
50-----	10	--do-----	Do.
50-----	10	Drench--	Irritation effect after 2, 6-percent weight loss. ³
100-----	3	Capsule--	Poisoned and died.
Sheep:			
10-----	10	--do-----	NIE.
10-----	10	--do-----	Do.
25-----	10	--do-----	Do.
25-----	10	--do-----	5-percent weight loss, chronic toxicity and death. ⁴
50-----	10	--do-----	NIE.
50-----	10	--do-----	9-percent weight loss.
100-----	3	--do-----	Poisoned and died.
Chickens: ⁵			
100-----	10	--do-----	51-percent weight gain.
250-----	10	--do-----	37-percent weight gain.
500-----	10	--do-----	39-percent weight gain.
Controls--	-----	-----	50-percent weight gain.

¹ Pyramin®, 80 percent wettable powder of pyrazon, Amchem Products, Inc., Ambler, Pa.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Apparently recovered, then 90 days after last dose, convulsions and death.

⁵ Average results of 5 treated chickens.

piratory mucosa was congested, the cranial vessels were engorged, and there were petechiae in the subcutaneous tissue. Chickens had edematous kidneys, enlarged spleen, and reddened intestinal mucosa.

Application rates for fenac for sugarcane range from 3.6 to 8 pounds actual per acre. The maximum rate would be hazardous for cattle, but not for sheep and chickens.

TABLE 39.—*Results of multiple oral dosing of cattle, sheep, and chickens with 2,4-dichlorophenyl p-nitrophenyl ether*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
50-----	10	Capsule--	NIE.
50-----	10	--do-----	Do.
100-----	6	--do-----	Poisoned after 3 and survived.
Sheep:			
50-----	10	--do-----	NIE.
50-----	10	--do-----	Do.
100-----	10	Drench--	Poisoned after 5 and survived, 11-percent weight loss.
100-----	10	Capsule--	Poisoned after 8, 13-percent weight loss, sacrificed.
100-----	10	--do-----	Poisoned after 3 and died 13 days after last dose, 15-percent weight loss.
Chickens: ³			
50-----	10	--do-----	62-percent weight gain.
100-----	10	--do-----	52-percent weight gain.
175-----	10	--do-----	19-percent weight loss.
250-----	10	--do-----	2 died after 9, 30-percent weight loss in survivors.
500-----	10	--do-----	4 died 6 to 8, 34-percent weight loss in survivor.
Controls--			54-percent weight gain.

¹ TOK WP-50®, 50 percent wettable powder of nitrofen, Rohm and Haas Co., Philadelphia, Pa.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

S-ethyl hexahydro-1*H*-azepine-1-carbothioate (molinate)

All test animals were dosed by capsule (table 42). Two yearlings were poisoned after one and six doses at 50 mg./kg., but another yearling was not affected by this same dosage. One sheep was poisoned after one dose at 75 mg./kg. One group of chickens had reduced weight gains at 25 mg./kg., but the same dosage had no adverse effects on another group.

Signs of poisoning in cattle and sheep were salivation, anorexia, diarrhea, and ataxia. One

sheep had tympanites and another had lethargy and muscular spasms.

At necropsy, the mucosa of the abomasum and intestines was hemorrhagic and lymph nodes were congested. The liver was swollen and often light brown. The spleen was distended and the kidneys were engorged with blood. The respiratory mucosa was often reddened and the thyroid was congested. Chickens had swollen, congested kidneys, light-brown liver, distended gall bladder, and reddened intestinal mucosa.

The application rate for molinate for rice is 3 pounds actual per acre. This rate would be hazardous for chickens, but not for cattle and sheep.

TABLE 40.—*Results of multiple oral dosing of cattle, sheep, and chickens with dimethyl tetrachloroterephthalate*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
100-----	10	Capsule--	NIE.
100-----	10	--do-----	Do.
250-----	10	--do-----	Poisoned after 5 and survived, 9-percent weight loss.
Sheep:			
25-----	10	--do-----	NIE.
25-----	10	--do-----	Do.
50-----	10	--do-----	Do.
50-----	10	--do-----	8-percent weight loss.
100-----	10	--do-----	NIE.
100-----	10	--do-----	Do.
175-----	10	--do-----	Do.
250-----	10	Drench--	Do.
375-----	10	--do-----	Do.
500-----	10	--do-----	Do.
Chickens: ³			
100-----	10	Capsule--	51-percent weight gain.
250-----	10	--do-----	49-percent weight gain.
500-----	10	--do-----	37-percent weight gain.
Controls--			54-percent weight gain.

¹ Dachthal W-75®, 75 percent wettable powder of DCPA, Diamond Shamrock Chemical Co., Cleveland, Ohio.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid (endothall), potassium salt

Cattle and sheep were dosed by capsule, chickens by pipette (table 43). A yearling was

TABLE 41.—*Results of multiple oral dosing of cattle, sheep, and chickens with (2,3,6-trichlorophenyl)acetic acid, sodium salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
25-----	10	Capsule--	NIE.
25-----	10	do-----	Do.
50-----	10	Drench--	Poisoned after 1 and survived, 7-percent weight loss. ³
50-----	10	Capsule--	Poisoned after 2 and survived, 14-percent weight loss.
100-----	10	do-----	NIE.
100-----	10	Drench--	Poisoned after 3 and survived, 10-percent weight loss.
Sheep:			
50-----	10	do-----	NIE.
100-----	10	do-----	Do.
100-----	10	do-----	Do.
175-----	4	do-----	Poisoned after 2 and survived, alopecia after 30 days, 14-percent weight loss.
250-----	4	do-----	Poisoned and died.
250-----	3	do-----	Do.
Chickens: ⁴			
100-----	10	Pipette--	52-percent weight gain.
175-----	10	do-----	1 died after 7, 16-percent weight gain in survivors.
250-----	10	do-----	1 died after 6, 47-percent weight gain in survivors.
500-----	10	do-----	4 died 1 to 6, 69-percent weight gain in survivor.
Controls--	-----	-----	54-percent weight gain.

¹ Fenac, 16.1 percent water soluble concentrate, Amchem Products, Inc., Ambler, Pa.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

poisoned after two doses at 25 mg./kg., and a sheep had weight loss at 10. One group of chickens had reduced weight gains at 10 and 25 mg./kg., but higher dosages had no adverse effects on other groups.

Signs of poisoning in sheep varied. The sheep with only weight loss appeared normal through-

TABLE 42.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with S-ethyl hexahydro-1H-azepine-1-carbothioate*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
25-----	10	NIE.
25-----	10	Do.
50-----	10	Do.
50-----	10	Poisoned after 6 and survived, 13-percent weight loss.
50-----	4	Poisoned after 1 and survived, 5-percent weight loss.
100-----	2	Poisoned after 1 and survived, 11-percent weight loss.
100-----	1	Poisoned and survived, 6-percent weight loss.
250-----	1	Poisoned and survived, 7-percent weight loss.
Sheep:		
50-----	10	NIE.
50-----	10	Do.
75-----	10	Poisoned after 1 and survived.
100-----	7	Poisoned after 1 and died.
100-----	2	Poisoned after 1 and died 2 days after last dose.
250-----	1	Poisoned and died.
Chickens: ³		
10-----	10	55-percent weight gain.
25-----	10	54-percent weight gain.
25-----	10	36-percent weight gain.
50-----	10	29-percent weight gain.
100-----	10	28-percent weight gain.
175-----	10	26-percent weight gain.
250-----	10	3 died after 4 to 7, 25-percent weight gain in survivors.
375-----	4	All died after 3 to 4.
500-----	4	Do.
Controls--	-----	48-percent weight gain.

¹ Ordram 6E®, 71 percent emulsifiable concentrate of molinate, Stauffer Chemical Co., New York, N.Y.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

TABLE 43.—*Results of multiple oral dosing of cattle, sheep, and chickens with 7-oxabicyclo [2.2.1]heptane-2,3-dicarboxylic acid, potassium salt*¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
10-----	10	Capsule--	NIE.
10-----	10	..do-----	Do.
25-----	3	..do-----	Poisoned after 2 and died 1 day after last dose.
Sheep:			
5-----	10	..do-----	NIE.
5-----	10	..do-----	Do.
10-----	10	..do-----	13-percent weight loss.
25-----	5	..do-----	Poisoned after 2 and died.
50-----	2	..do-----	Poisoned and died.
Chickens: ³			
10-----	10	Pipette---	48-percent weight gain.
25-----	10	..do-----	50-percent weight gain.
50-----	10	..do-----	57-percent weight gain.
100-----	10	..do-----	56-percent weight gain.
250-----	10	..do-----	55-percent weight gain.
Controls----			55-percent weight gain.

¹ Potassium Endothal®, 40.3 percent water soluble concentrate of endothall, Pennwalt Corp., Philadelphia, Pa.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

out the trial, but the sheep more severely affected had anorexia and diarrhea. The yearling had anorexia and ataxia, with vomition and salivation.

At necropsy, the abomasal and intestinal mucosa was hemorrhagic, the liver was swollen, and the gall bladder was distended. The kidneys were congested and there was excessive edematous fluid in the peritoneal cavity. The adrenals were enlarged, with congested cortex in one sheep. The spleen was thickened with dark, semiliquid contents in the yearling.

Application rates for endothall range from 1 to 6.55 pounds actual per acre. These rates would be hazardous for sheep, but not for chickens. Rates of 3 pounds or greater would be hazardous for cattle.

2-chloro-N-isopropylacetanilide (propachlor)

All test animals were dosed by capsule (table 44). A yearling was poisoned after three doses at 25 mg./kg. One sheep was poisoned after nine doses at 10 mg./kg., but two others were not affected by this dosage. Chickens had reduced weight gains at 25 mg./kg.

Signs of poisoning were anorexia and occasional diarrhea in cattle and sheep.

At necropsy on the sheep, there were a friable, congested liver, reddened intestinal mucosa, and hemorrhages in the abdominal wall. In chickens, there were congested kidneys,

TABLE 44.—*Results of multiple oral dosing by capsule of cattle, sheep, and chickens with 2-chloro-N-isopropylacetanilide*¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	<i>Number</i>	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
25-----	10	Poisoned after 3 and survived, 13-percent weight loss.
Sheep:		
5-----	10	NIE.
5-----	10	Do.
10-----	10	Do.
10-----	10	Do.
10-----	10	Poisoned after 9 and survived, 6-percent weight loss.
25-----	10	NIE.
25-----	10	Poisoned after 2 and died.
50-----	10	Poisoned after 4 and survived, 22-percent weight loss.
Chickens: ³		
5-----	10	53-percent weight gain.
10-----	10	50-percent weight gain.
25-----	10	34-percent weight gain.
50-----	10	32-percent weight gain.
100-----	5	All died after 3 to 5.
Controls----		55-percent weight gain.

¹ Ramrod 65®, 65 percent wettable powder of propachlor, Monsanto Co., St. Louis, Mo.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

swollen, engorged liver, and hemorrhagic intestinal mucosa.

Application rates for propachlor range from 3.9 to 6 pounds actual per acre. These rates would be hazardous for the three test species.

O-(2,4-dichlorophenyl) O-methyl isopropylphosphoroamidothioate (DMPA)

All test animals were dosed by capsule (table 45). One yearling and two sheep had weight losses at 10 mg./kg. One group of chickens had reduced weight gains at this dosage level, but that same dosage had no adverse effects on another group.

Signs of poisoning in cattle and sheep varied among the affected animals. The signs were notably absent in most cases that were less severe; however, one sheep in this category died 6 days after the last dose at 25 mg./kg. Other animals had anorexia, diarrhea, ataxia, and excessive salivation. One yearling developed swollen joints, followed by paraplegia and unilateral keratitis, and died 26 days after the last dose at 25 mg./kg.

At necropsy, the liver and kidneys were congested and the gastrointestinal mucosa was hemorrhagic. The cranial vessels were usually engorged and prominent. In one sheep the pancreas was reddened.

There is no current registration for DMPA in agriculture. Application rates in excess of 1 pound actual per acre would be hazardous for the three test species.

3-amino-2,5-dichlorobenzoic acid (chloramben)

Cattle were dosed by capsule or drench, sheep by capsule, chickens by pipette (table 46). One yearling was drenched at 25 mg./kg. and developed a mandibular swelling after eight doses, with weight loss. Because other cattle were unaffected by capsule at this and higher dosages, this sign was not considered true toxicity of chloramben to this species. Another yearling had a weight loss at 175 mg./kg. The same reactions followed sheep trials, with weight loss at 25 mg./kg. and evidence of poisoning at 50, but dosages up to and including 500 had no

TABLE 45.—Results of multiple oral dosing by capsule of cattle, sheep, and chickens with O-(2,4-dichlorophenyl) O-methyl isopropylphosphoroamidothioate¹

Animal and dosage received (mg./kg.)	Doses	Results and remarks ²
	Number	
Cattle:		
10-----	10	NIE.
10-----	10	Do.
10-----	10	Do.
10-----	10	9-percent weight loss.
25-----	6	Poisoned after 2 and died 26 days after last dose, 10-percent weight loss.
25-----	6	Poisoned after 3 and died 5 days after last dose.
Sheep:		
5-----	10	NIE.
10-----	10	Do.
10-----	10	Do.
10-----	10	5-percent weight loss.
10-----	10	5-percent weight loss.
25-----	10	11-percent weight loss.
25-----	10	NIE during trial, died 6 days after last dose.
25-----	10	Poisoned after 5 and died.
50-----	5	Poisoned and died.
50-----	4	Poisoned after 2 and died.
Chickens: ³		
5-----	10	55-percent weight gain.
10-----	10	51-percent weight gain.
10-----	10	35-percent weight gain.
25-----	10	48-percent weight gain.
25-----	10	27-percent weight gain.
50-----	10	34-percent weight gain.
100-----	10	1 died after 10, 18-percent weight gain in survivors.
Controls----	-----	54-percent weight gain.

¹ Crab Grass Killer with Zytron®, 35 percent emulsifiable concentrate of DMPA, Dow Chemical Co., Midland, Mich.

² NIE indicates no ill effects apparent.

³ Average results of 5 treated chickens.

further adverse effects on other test animals. One group of chickens had reduced weight gains at 375 mg./kg., but that same dosage had no adverse effects on another group.

Signs of poisoning in one sheep were anorexia

TABLE 46.—Results of multiple oral dosing of cattle, sheep, and chickens with 3-amino-2,5-dichlorobenzoic acid ¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
10-----	10	Capsule--	NIE.
25-----	10	--do-----	Do.
25-----	8	Drench--	Irritation effect after 8, 9-percent weight loss. ³
50-----	10	Capsule--	NIE.
100-----	10	--do-----	Do.
175-----	10	--do-----	Do.
175-----	10	--do-----	6-percent weight loss.
250-----	10	--do-----	NIE.
250-----	10	--do-----	5-percent weight loss.
Sheep:			
10-----	10	Drench--	NIE.
25-----	10	--do-----	Do.
25-----	10	--do-----	5-percent weight loss.
50-----	10	--do-----	NIE.
50-----	10	--do-----	Poisoned after 2 and survived, 10-percent weight loss.
100-----	10	--do-----	NIE.
100-----	10	--do-----	Do.
175-----	10	--do-----	Do.
250-----	10	--do-----	Do.
375-----	10	--do-----	Do.
500-----	10	--do-----	Do.
Chickens: ⁴			
100-----	10	Pipette--	50-percent weight gain.
250-----	10	--do-----	49-percent weight gain.
375-----	10	--do-----	52-percent weight gain.
375-----	10	--do-----	32-percent weight gain.
500-----	10	--do-----	2 died after 7 and 9, 51-percent weight gain in survivors.
Controls--	-----	-----	46-percent weight gain.

¹ Vegiben®, 23.4 percent emulsifiable concentrate of chloramben, Amchem Products, Inc., Ambler, Pa.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

TABLE 47.—Results of multiple oral dosing of cattle, sheep, and chickens with 3-amino-s-triazole ¹

Animal and dosage received (mg./kg.)	Doses	Means of dosing	Results and remarks ²
	<i>Number</i>		
Cattle:			
10-----	10	Capsule--	NIE.
10-----	10	--do-----	Do.
25-----	10	Drench--	Poisoned after 6 and survived, 7-percent weight loss. ³
25-----	10	--do-----	Poisoned after 3 and survived, 8-percent weight loss.
50-----	6	Capsule--	Poisoned after 2 and survived, 16-percent weight loss.
Sheep:			
5-----	10	Drench--	NIE.
10-----	10	--do-----	Do.
10-----	10	--do-----	9-percent weight loss.
25-----	10	--do-----	NIE.
25-----	10	--do-----	5-percent weight loss.
25-----	9	--do-----	Poisoned after 3 and died 2 days after last dose, 24-percent weight loss.
50-----	10	--do-----	Poisoned after 3 and survived, 7-percent weight loss.
50-----	10	--do-----	Poisoned after 2, 24-percent weight loss, sacrificed 7 days after last dose.
Chickens: ⁴			
50-----	10	Pipette--	54-percent weight gain.
100-----	10	--do-----	43-percent weight gain.
250-----	10	--do-----	60-percent weight gain.
250-----	10	--do-----	36-percent weight gain.
375-----	7	--do-----	All died after 3 to 7.
500-----	4	--do-----	All died after 3 to 4.
Controls--	-----	-----	51-percent weight gain.

¹ Amitrol®, 21.1 percent water soluble concentrate of amitrole, Amchem Products, Inc., Ambler, Pa.

² NIE indicates no ill effects apparent.

³ Affected by chemical reaction of the formulation on the pharyngeal mucosa, resulting in mandibular area enlargement accompanied by partial anorexia and dyspnea.

⁴ Average results of 5 treated chickens.

and depression. An uneventful recovery followed the dosing regimen.

At necropsy on two chickens, there were hemorrhages in the spleen, congested liver and kidneys, and reddened intestinal mucosa.

Application rates for chloramben range from 2 to 4.1 pounds actual per acre. These rates would not be hazardous for the three test species.

3-amino-s-triazole (amitrole)

Cattle were dosed by capsule or drench, sheep by drench, chickens by pipette (table 47). Two yearlings were poisoned after three and six doses at 25 mg./kg., and one sheep had weight loss at 10. Chickens had significant reduced weight gains at 100 mg./kg.

Anorexia was seen in cattle and in a few of the sheep at some of the higher dosages tested; two sheep showed weight losses without any abnormal signs. The yearling dosed at 50 mg./kg. also had ataxia and weakness before dosing was discontinued after six doses; a full recovery followed.

At necropsy, there were hemorrhages in the abomasal and intestinal mucosa, congested lungs and upper respiratory tract, swollen, friable liver, and blood-engorged kidneys. Chickens had reddened intestinal mucosa and congested liver and kidneys.

Application rates for amitrole range from 1 to 4 pounds actual per acre. The maximum would be hazardous for cattle and sheep, but not for chickens.

CONCLUSION

These data have been abstracted in table 48, "Summary of dosages of various organic herbi-

cides that cause significant weight loss, reduced weight gain, or poisoning in cattle, sheep, and chickens."

TABLE 48.—Summary of dosages of various organic herbicides that cause significant weight loss, reduced weight gain, or poisoning in cattle, sheep, and chickens¹

Herbicide	Dosage rate	Least number of dosages for—			Herbicide	Dosage rate	Least number of dosages for—		
		Cattle	Sheep	Chickens			Cattle	Sheep	Chickens
Chlorophenoxy compounds: (2,4-dichlorophenoxy)acetic acid (2,4-D), dimethylamine salt.	Mg./kg.					Mg./kg.			
	500			2	[(4-chloro- <i>o</i> -tolyl)oxy]acetic acid (MCPA), dimethylamine salt.	500			4
	375			10		375		3	
	250			10		250	8	5	7
	175	10	3	10		175	10		
	100	10	2	10		100		10	5
(2,4-dichlorophenoxy)acetic acid (2,4-D), 2-ethylhexyl ester.	500			10	4-(2,4-dichlorophenoxy)butyric acid (2,4-DB), dimethylamine salt.	500			10
	250			10		250			10
	100	6	5	10		100			10
	50		10			50			10
									10
(2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), 2-ethylhexyl ester.	500			8	Chlorinated aliphatic acid compounds: 2-(2,4,5-trichlorophenoxy)ethyl 2,2-dichloropropionate and related compounds (carbon).	500			1
	375			9		250	2	5	10
	250	7	4	10		100			
	175		7			50			
	100	10	2	10					
(2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), triethylamine salt.	500			2	2-[(4-chloro- <i>o</i> -tolyl)oxy]propionic acid (mecoprop), diethanolamine salt.	500			4
	375			2		375			2
	250	3	4	9		250	2	2	5
	175	1	4			175	5		
	100	10	2	10		100			10
4-[(4-chloro- <i>o</i> -tolyl)oxy]butyric acid (MCPB), sodium salt.	50		5	10	trichloroacetic acid (TCA), sodium salt. ²	50			10
	250			6		375			
	100	1	5	10		250	3	2	
	50		5			175		2	
						50	10	10	
[(4-chloro- <i>o</i> -tolyl)oxy]acetic acid (MCPA), sodium salt.	500			1		375			
	250	8	3			250			
	175	3	10			175			
	100		5			50			

TABLE 48.—Summary of dosages of various organic herbicides that cause significant weight loss, reduced weight gain, or poisoning in cattle, sheep, and chickens ¹—(Continued)

Herbicide	Dosage rate	Least number of dosages for—		
		Cattle	Sheep	Chickens
Thiocarbamate compounds—Con. 2-chloroallyl diethylthiocarbamate (CDEC).	Mg./kg.			
	250	—	—	10
	175	—	—	7
	100	—	—	10
Arsenical compounds: monosodium methanearsonate (MSMA).	50	—	1	—
	25	1	3	—
	250	—	—	10
	100	—	2	10
disodium methanearsonate (DSMA)	50	2	3	—
	25	2	—	—
	10	2	—	—
	500	—	—	10
hydroxydimethylarsine oxide (cacodylic) acid.	375	—	—	10
	25	2	5	—
	500	—	—	10
	250	—	—	10
Substituted dinitroaniline compounds: <i>a,a,a</i> -trifluoro-2,6-dinitro- <i>N,N</i> -dipropyl- <i>p</i> -toluidine (trifluralin).	175	—	—	10
	100	—	—	10
	50	1	2	—
	25	8	10	—
<i>N</i> -butyl- <i>N</i> -ethyl- <i>a,a,a</i> -trifluoro-2,6-dinitro- <i>p</i> -toluidine (benefin).	500	—	—	10
	250	—	—	10
	175	2	2	—
	250	—	—	9
Phthalamic acid compounds: <i>N</i> -1-naphthylphthalamic acid (naptalam), sodium salt. <i>N</i> -1-naphthylphthalamic acid (naptalam) and 2- <i>sec</i> -butyl-4,6-dinitrophenyl (dinoseb).	175	—	—	10
	100	—	—	10
	50	2	2	—
	25	6	—	—
4-(methylsulfonyl)-2,6-dinitro- <i>N,N</i> -dipropylaniline (nutralin). ²	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Dipyridyl compounds: 1,1'-dimethyl-4,4'-bipyridium ion (paraquat), methylsulfate salt.	50	—	—	—
	25	4	3	—
	10	10	10	—
	250	—	—	—
6,7-dihydrodipyrido[1,2- <i>a</i> :2',1'- <i>c</i>]pyrazinedium ion (diquat), dibromide salt.	175	—	—	—
	100	—	—	—
	50	—	1	—
	25	3	3	—
Phthalamic acid compounds: <i>N</i> -1-naphthylphthalamic acid (naptalam), sodium salt. <i>N</i> -1-naphthylphthalamic acid (naptalam) and 2- <i>sec</i> -butyl-4,6-dinitrophenyl (dinoseb).	10	2	—	—
	5	8	—	—
	500	—	—	—
	250	—	—	—
Least number of dosages for—	175	—	—	—
	100	—	—	—
	50	—	—	—
	25	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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	100	—	—	—
Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
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Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175	—	—	—
	100	—	—	—
Least number of dosages for—	500	—	—	—
	250	—	—	—
	175</			

	<i>Mg./kg.</i>				<i>Mg./kg.</i>				
Miscellaneous compounds: tris[2-(2,4-dichlorophenoxy)ethyl] phosphite (2,4-DEP).	500	---	---	2	S-ethyl hexahydro-1 <i>H</i> -azepine- 1-carbothioate (molinate).	500	---	---	3
	375	---	---	8		375	---	---	3
	250	---	---	10		250	1	1	4
	100	2	2	10		175	---	---	10
	50	2	2	10		100	1	1	10
5-amino-4-chloro-2-phenyl-3(2 <i>H</i>)- pyridazinone (pyrazon).	25	10	10	10	7-oxabicyclo[2.2.1]heptane- 2,3-dicarboxylic acid (endothall), potassium salt.	75	---	---	10
	10	---	10	---		50	1	---	10
	500	---	---	10		25	---	---	10
	250	---	---	10		50	---	2	10
	100	3	3	---		25	2	2	10
2,4-dichlorophenyl <i>p</i> -nitrophenyl ether (nitrofen).	50	---	---	---	2-chloro- <i>N</i> -isopropylacetanilide (propachlor).	10	---	---	3
	175	---	---	---		50	---	4	10
	100	3	3	---		25	3	2	10
	500	---	---	6		10	---	9	10
	250	---	---	9		---	---	---	---
dimethyl tetrachloroterephthalate (DCPA).	100	---	---	10	<i>O</i> -(2,4-dichlorophenyl) <i>O</i> -methyl isopropylphosphoramidothioate (DMPA).	100	---	---	10
	500	---	---	10		50	---	2	10
	250	5	---	10		25	2	5	10
	50	---	10	---		10	10	10	10
	---	---	---	---		---	---	---	---
(2,3,6-trichlorophenyl)acetic acid (fenac), sodium salt.	500	---	---	1	3-amino-3-triazole (amitrole)	500	---	---	7
	250	---	3	6		375	---	---	10
	175	---	2	7		250	10	---	10
	100	3	---	---		175	10	---	10
	50	1	---	---		50	---	2	2
						25	---	3	10

¹ Broken lines indicate that either the herbicide was not tested at that rate or the herbicide was not toxic to the animal at that rate.

² No toxic dosages found for chickens.

